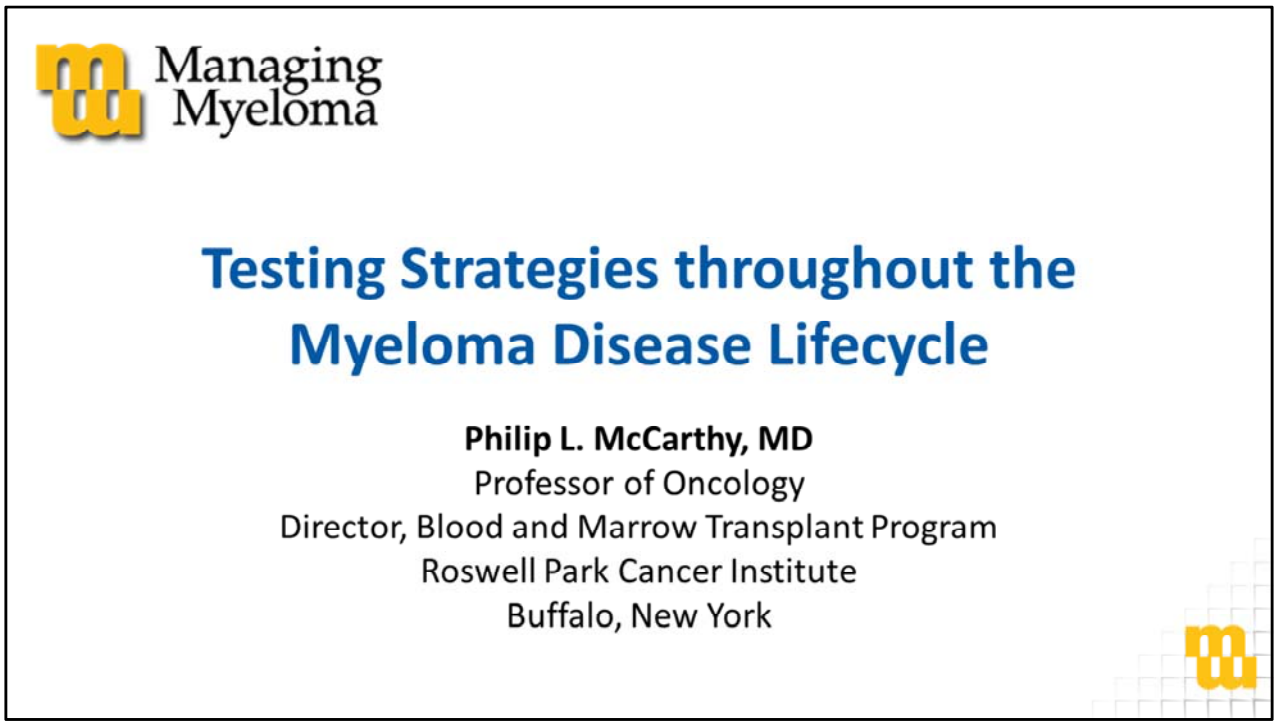
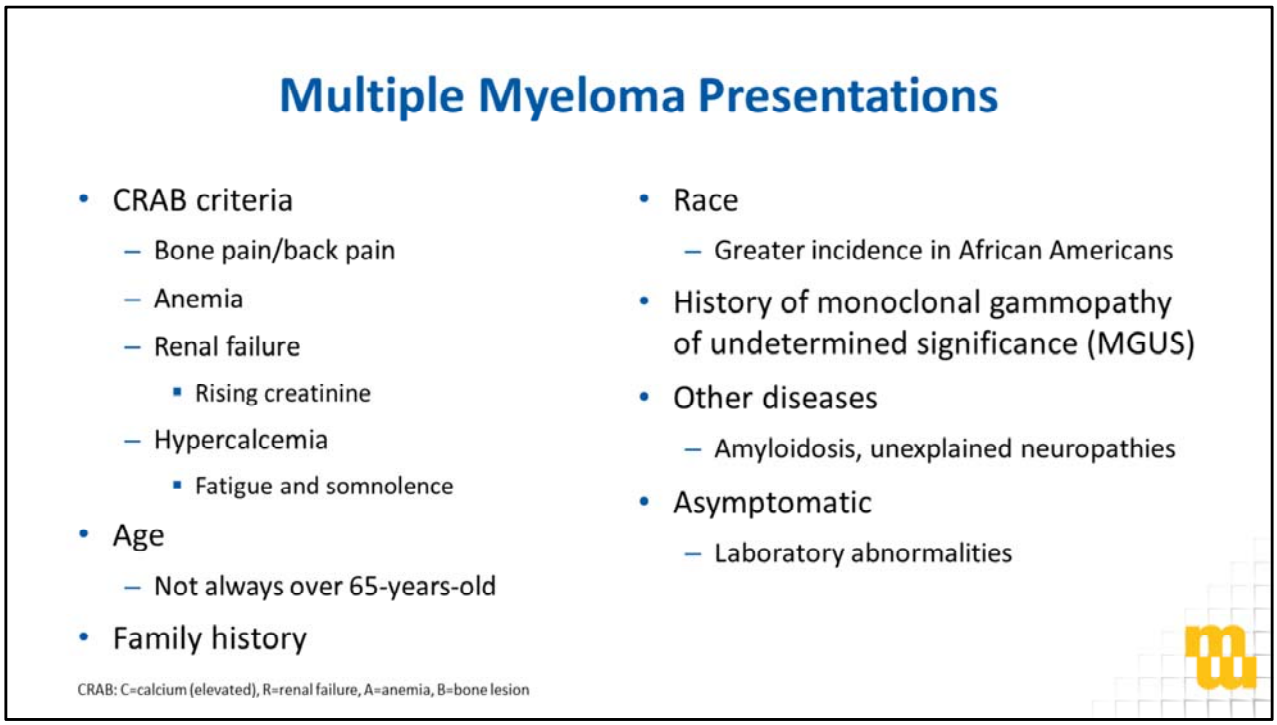
Testing Strategies throughout the Myeloma Disease Lifecycle



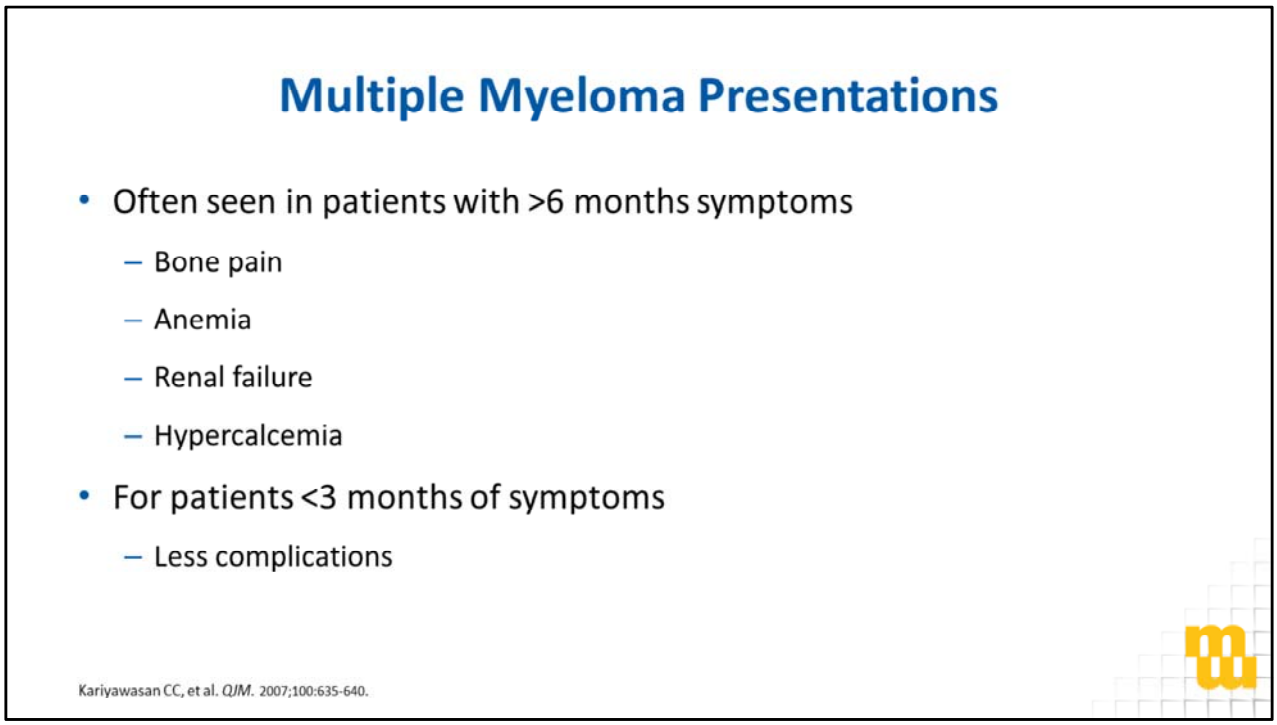
Welcome to *Managing Myeloma*, I am Dr. Philip McCarthy. In today's presentation, I will be reviewing testing strategies throughout the myeloma disease lifecycle. I will begin with presenting symptomatology and diagnostic recommendations for patients suspected of having multiple myeloma, including prognostic tests to be considered as part of the initial workup. I will conclude my presentation with the discussion of patients who relapsed from complete remission as well as those who developed frank disease progression. So, let's begin.

Testing Strategies throughout the Myeloma Disease Lifecycle



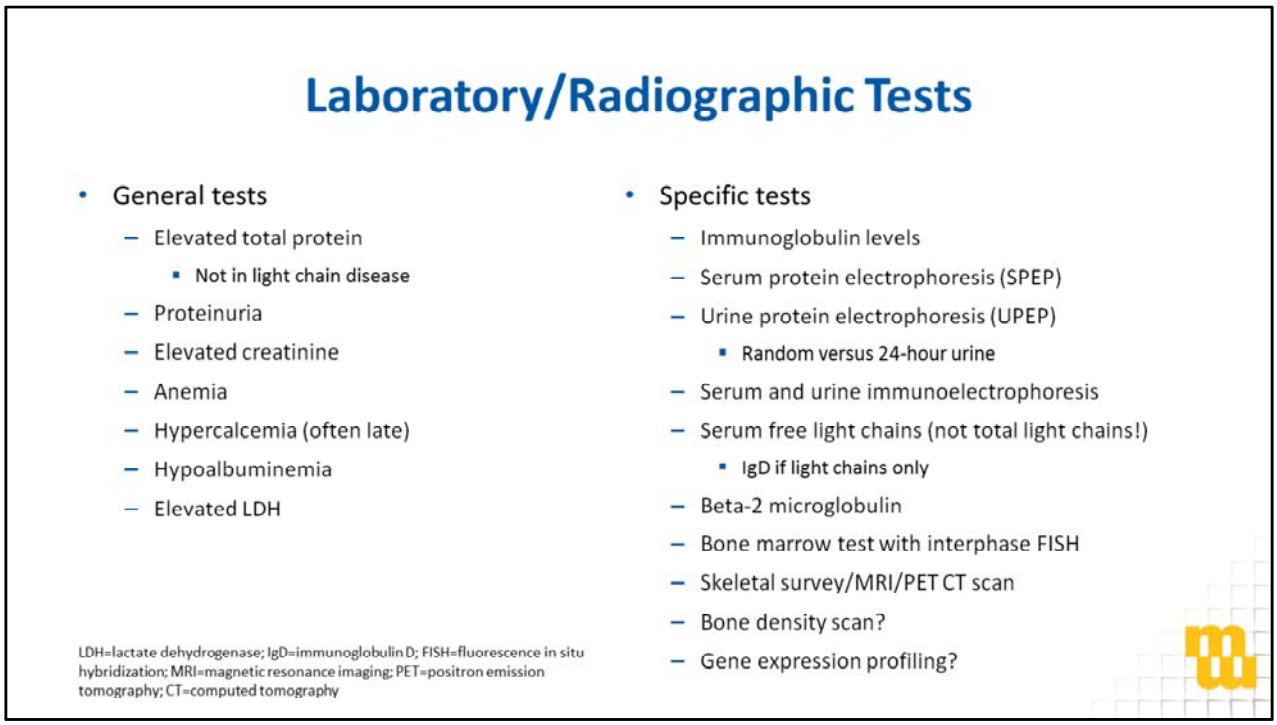
On the left hand column, you will see the standard CRAB criteria for presentation, and these are patients who usually have fairly advanced disease. They will present with bone pain or back pain, anemia, renal failure, as manifested by rising creatinine, and hypercalcemia often with the symptoms of fatigue and somnolence. Now, age is something that people think about. The average age is approximately 70 years for a myeloma patient at presentation, but not all patients are above 65 to 70 years of age. We have had patients as young as in their late 20s present with multiple myeloma. So, it is something to be considered in the presentation, it is not always the older age patient. Family history can be important. Sometimes, myeloma will run in the family, and as well race. There is a greater incidence in African Americans, and it is often a more aggressive disease in the African American population. A lot of patients with myeloma will have a preexisting MGUS, or monoclonal gammopathy of undetermined significance. These have been present often for several years before developing full-blown multiple myeloma. There are sometimes other diseases that will present with myeloma including amyloidosis or unexplained neuropathy. In many cases, the patients will be asymptomatic, and in other words will only have laboratory abnormalities. Indeed this is something we would like to have happened more often because patients who presented with full-blown CRAB criteria often will have major impacts on their quality of life, especially if they have something such as a skeletal-related event leading to a fracture which causes significant morbidity.

Testing Strategies throughout the Myeloma Disease Lifecycle



We will often see patients with symptoms greater than 6 months having CRAB criteria. So, in other words, they will have been complaining about bone pain for several months. The patient will get a workup, but it may not address directly the bone pain and they may go and see somebody to have a spine manipulation but will not have any real testing done. Again, some patients will be tired and it will be a while before a complete blood count (CBC) is obtained to show that the patient is anemic, or else the creatinine is rising to account for fatigue, and in cases of altered mental status, calcium will be elevated. For patients who have symptoms for less than 3 months, they have less complications, which makes sense. In other words, the symptoms of the bone pain, anemia, renal failure, and hypercalcemia are addressed much quicker, leading to less complications.

Testing Strategies throughout the Myeloma Disease Lifecycle

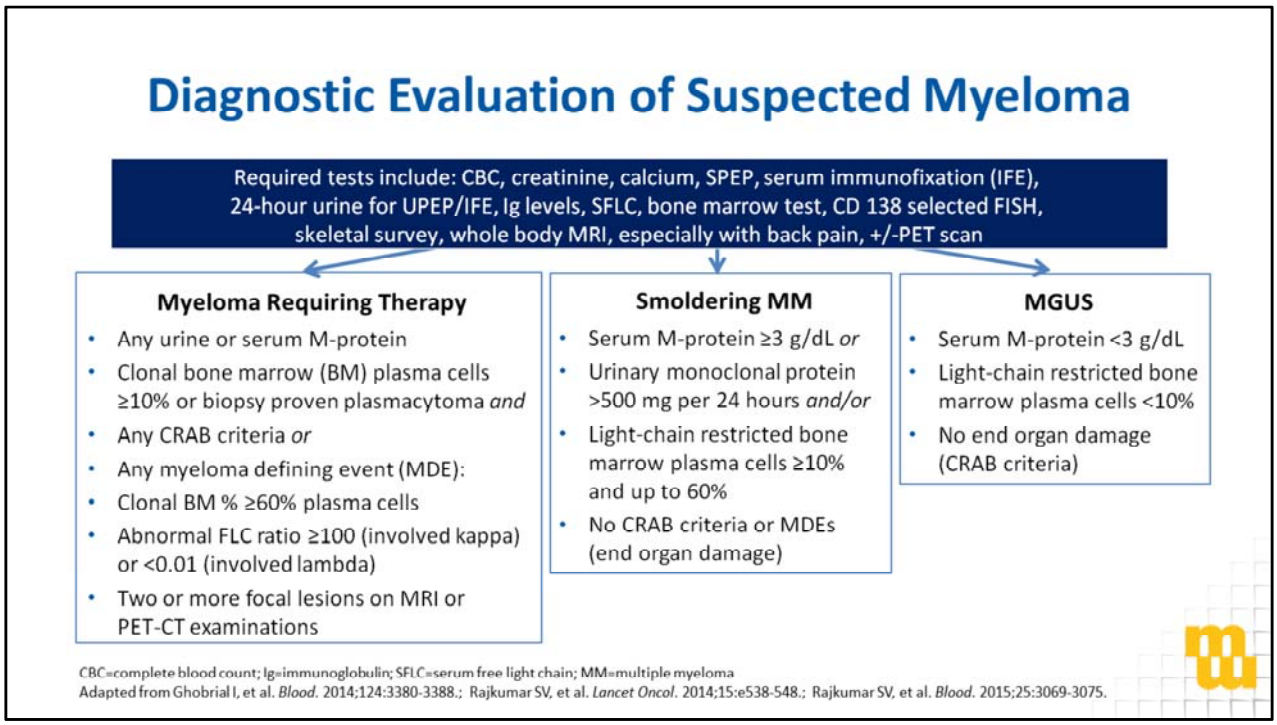


These are some of the laboratory and radiographic tests that should be considered. The general tests for somebody who is just being screened, oftentimes the only manifestation of the myeloma in an asymptomatic patient will be an elevated total protein. However, this is not seen in light chain disease because light chains are not a cause of an elevated total protein, they're primarily excreted in the urine. Thus, proteinuria will be a manifestation in patients who either have nephrotic syndrome due to a glomerular leak of the albumin due to the myeloma, or else the excessive excretion of light chains. Elevated creatinine will occur as the myeloma damages the kidney. This is something to be considered in a patient, for example, with diabetes, not to ascribe the rising creatinine to diabetes, but to think of myeloma as exclusion criteria when you are evaluating a patient developing renal failure. I mentioned earlier, there are many other causes of anemia, but myeloma should be considered during the workup. Hypercalcemia is an often late manifestation, as is the low albumin due to heavy burden of disease, as well as an LDH elevation which is seen in higher-risk disease. For specific tests, immunoglobulin levels usually IgA, IgG, and IgM are obtained. You will often see a rise in the IgA or IgG which are the more common myeloma proteins. In the serum protein electrophoresis, you will see the classic M-spike, and I will show you some pictures of that. The urine protein electrophoresis can be done either on a spot test, and that will pick up protein, especially if there is a large amount of it, but sometimes a 24-hour urine test needs to be done to pick up small amounts of protein in the urine, as well as the presence of albumin.

Testing Strategies throughout the Myeloma Disease Lifecycle

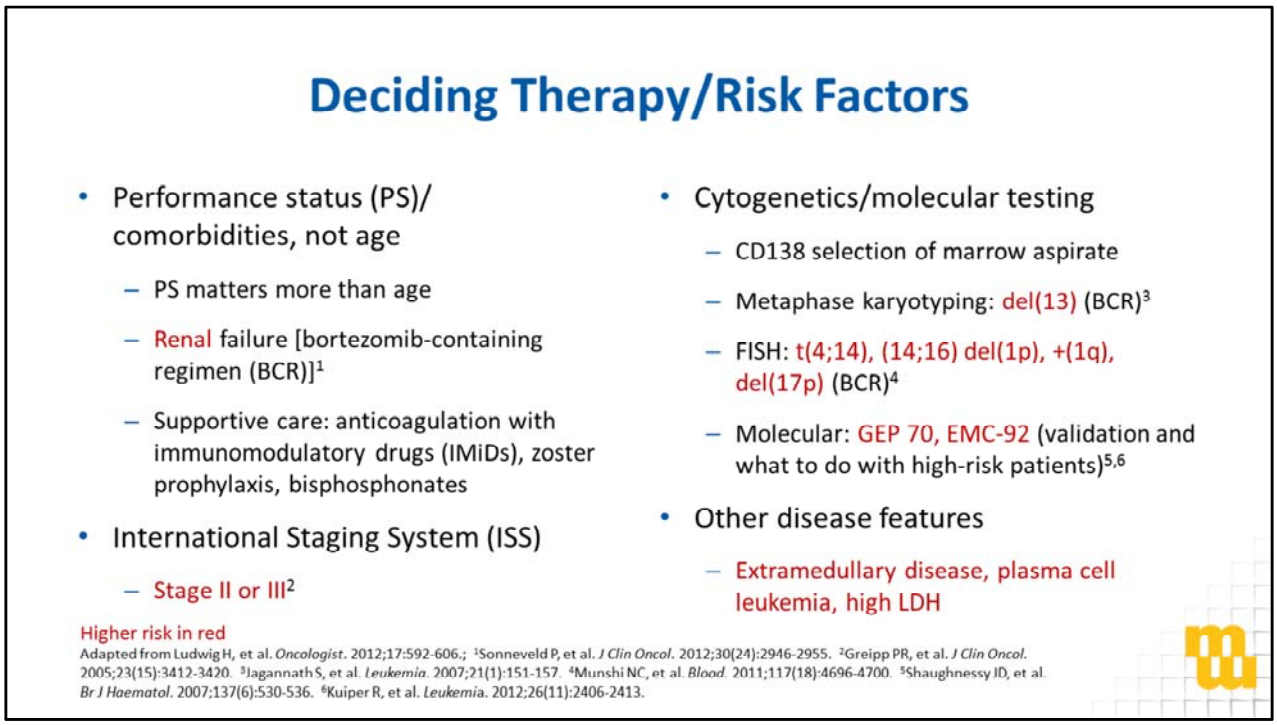
Then in immunoelectrophoresis, immunofixation is performed to identify the exact type of monoclonal protein, whether it is IgA, IgM, kappa, or lambda. One thing to remember is if the patient has light chain only disease is to test for IgD because IgD can be elevated in light chain disease and it is often not part of the routine testing. Other characteristics that are obtained are beta-2 microglobulin. I will show you how that is important. Bone marrow test with interphase FISH, skeletal survey, and MRI or PET scans are also obtained. Classically, we obtain skeletal surveys to look for lytic lesions, but now, MRI is the more sensitive test, especially in a patient who has back pain. The PET-CT will also help us find occult disease, especially if you suspect the patient has a higher burden disease and you are not seeing much on the skeletal survey in terms of abnormalities. A bone density scan can also be utilized. We do this sometimes in patients who we do not see lytic lesions, but there is a suspicion, that's a soft one, on the radiographic findings that the patient may have bone thinning. A bone density scan will tell you if your patient has accelerated osteoporosis due to the presence of multiple myeloma and is a candidate for early bisphosphonate use. Gene expression profiling is performed on the bone marrow and helps with some forms of risk stratification.

Testing Strategies throughout the Myeloma Disease Lifecycle



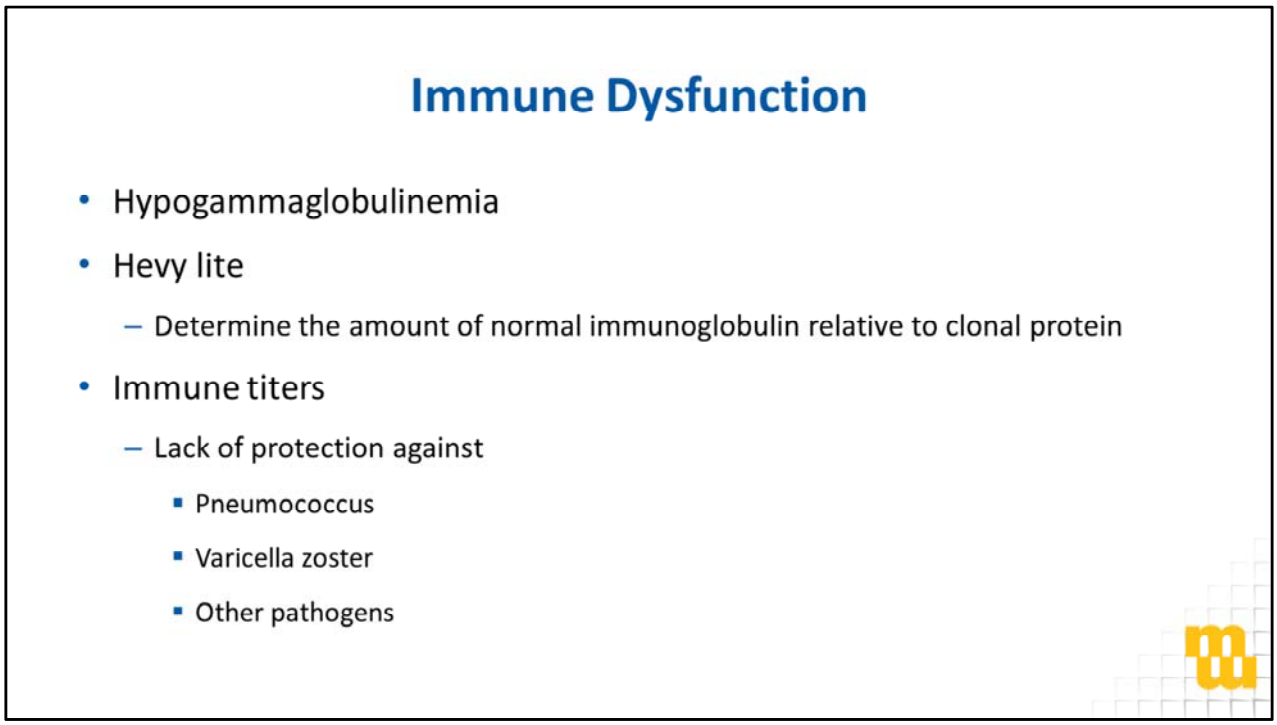
Now, this is a busy slide, but it summarizes what I talked to you about in the previous slide. All the tests are listed at the top ranging from the CBC, the chemistry panel, the SPEP, immunoelectrophoresis, as well as 24-hour urine, serum-free light chains, the bone marrow test, the iFISH, and the radiographic testing, be it skeletal survey, MRI, or PET scan. If you look in the far right-hand side for MGUS, these are patients who have a serum protein less than 3 g/dL, there is less than 10% clonal plasma cells in the marrow, and there is no end organ damage. These patients can be observed. Exceptions would be if the patient has, for example, amyloidosis, then that would be an indication for therapy. For smoldering myeloma, these are patients who have a higher level of protein greater than 3 g/dL or greater than 500 mg/24 hours in the urine test and/or light chain restricted bone marrow plasma cells that are between 10% and 60%. There are no CRAB criteria, nor are there any myeloma-defining events, and that is relatively new criteria which I will talk about on the left-hand side. For myeloma requiring therapy, you can have any level of urine or serum M-protein, but now, it is important that you have greater than 10% clonal plasma cells or a biopsy-proven plasmacytoma in CRAB criteria, or any myeloma-defining events. These are manifested by greater than 60% bone marrow plasma cells, and abnormal free light chain ratio of greater than 100 for kappa and less than 0.01 for lambda, and then, two or more focal lesions on MRI or PET-CT examination. The slide and criteria were adapted from Irene Ghobrial and Vincent Rajkumar's articles which are listed below.

Testing Strategies throughout the Myeloma Disease Lifecycle



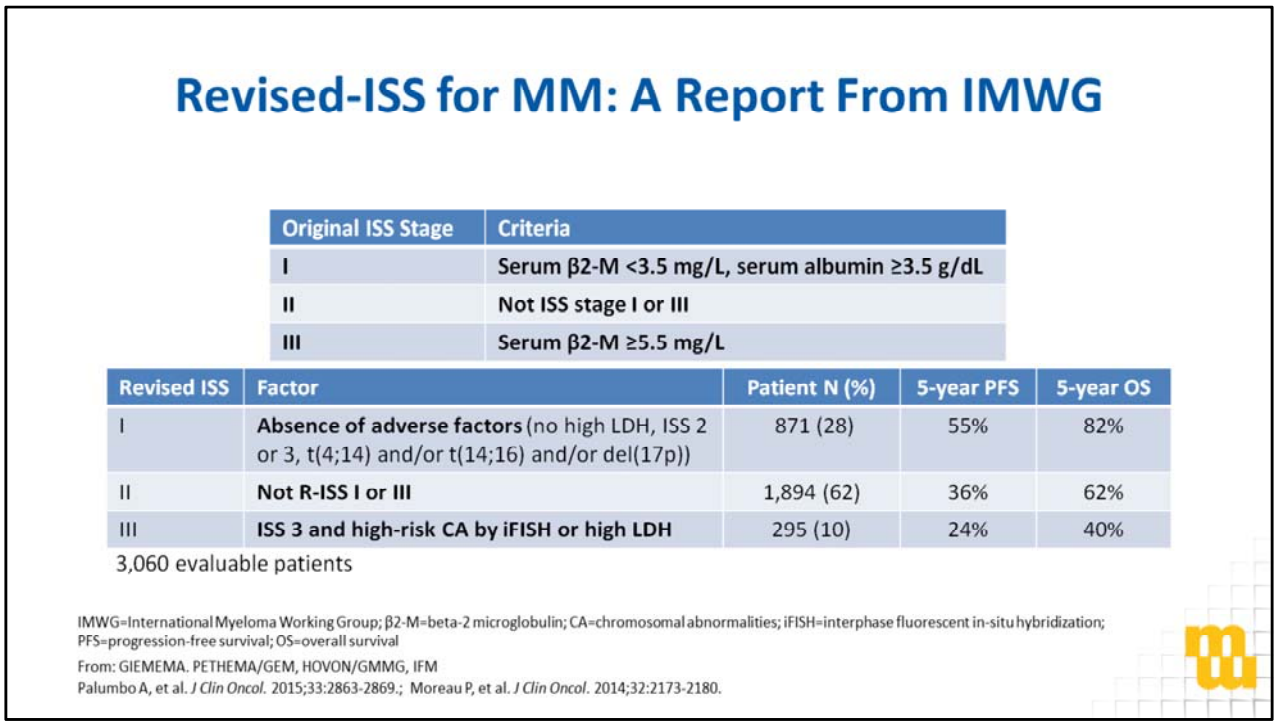
So, how do we decide therapy and risk factors? We often decide therapy based on performance status and comorbidities rather than age in that performance status really matters in terms of how well a patient will tolerate therapy. For a patient who is in renal failure, they often will have a decrease in performance status and it is important to remember that the proteasome inhibitors, in particular bortezomib, are considered a standard treatment for a patient with renal failure as opposed to most IMiDs which are cleared through the kidneys. Supportive care is very important: anticoagulation in patients receiving IMiDs, zoster prophylaxis for those who are receiving proteasome inhibitor, and bisphosphonates decrease the incidence and severity of skeletal-related events. The ISS, or the International Scoring System, is important for prognostication, I have a slide coming up that goes over that. Cytogenetics and molecular testing can emphasize the importance of a CD138 selection of the marrow aspirate as this pulls out the plasma cell selectively to do interphase FISH. Metaphase karyotyping is useful for deletion 13. It can be seen on that, but it is not always readily seen; it is better seen on FISH. It is important because deletion 13 often requires a proteasome inhibitor as part of the initial therapy. Listed below on FISH are t(4;14), t(14;16), deletion 1p, addition of 1q, or deletion 17 are all considered higher-risk, and the 14 abnormalities as well as 17 have been incorporated into a new scoring system. There are molecular tests that can be done. Gene expression profiling, GEP-70 or EMC-92, which do identify the very high-risk patient population. However, we are not sure how to aggressively treat these patients. It does again identify the high-risk population, but we need to develop better strategies for controlling these patients with very high-risk disease. Other high-risk features include extramedullary disease, plasma cell leukemia at presentation, or high LDH.

Testing Strategies throughout the Myeloma Disease Lifecycle



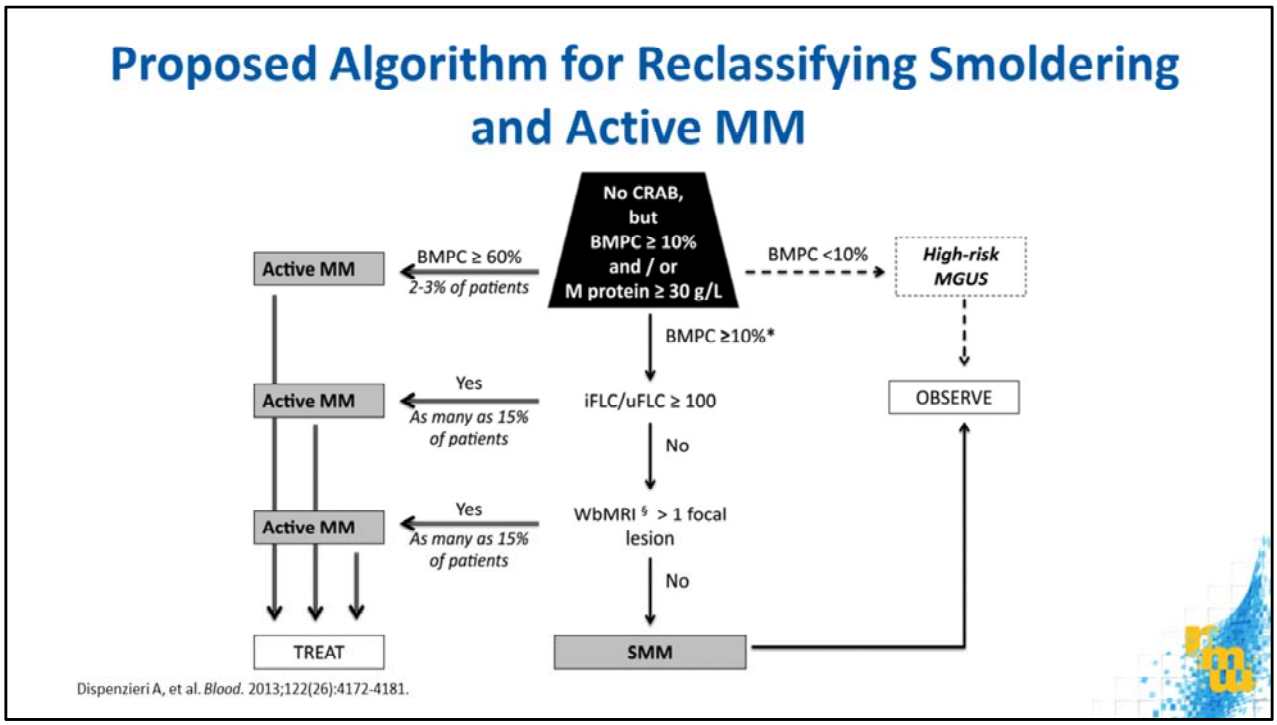
One other thing to consider is immune dysfunction. Patients will sometimes present with hypogammaglobulinemia or essentially immune paresis. There is a test called Hevylite, which sometimes allows you to determine the amount of normal immunoglobulin relative to clonal protein to tell you if there is suppression of the normal immunoglobulin production. Another way of seeing this is that patients will have lack of protection against a variety of pathogens. You will find that they no longer have protection against pneumococcus, varicella, tetanus, diphtheria, and that they may need to be revaccinated. So, if you have time, it is sometimes advisable to have the patient get vaccinated before they require therapy. If they require therapy right away, it is something that you will consider later on, but it is very important to note these patients could be at risk for infections because they do not have adequate immunity against standard pathogens for which patients received vaccinations as both children and adults.

Testing Strategies throughout the Myeloma Disease Lifecycle



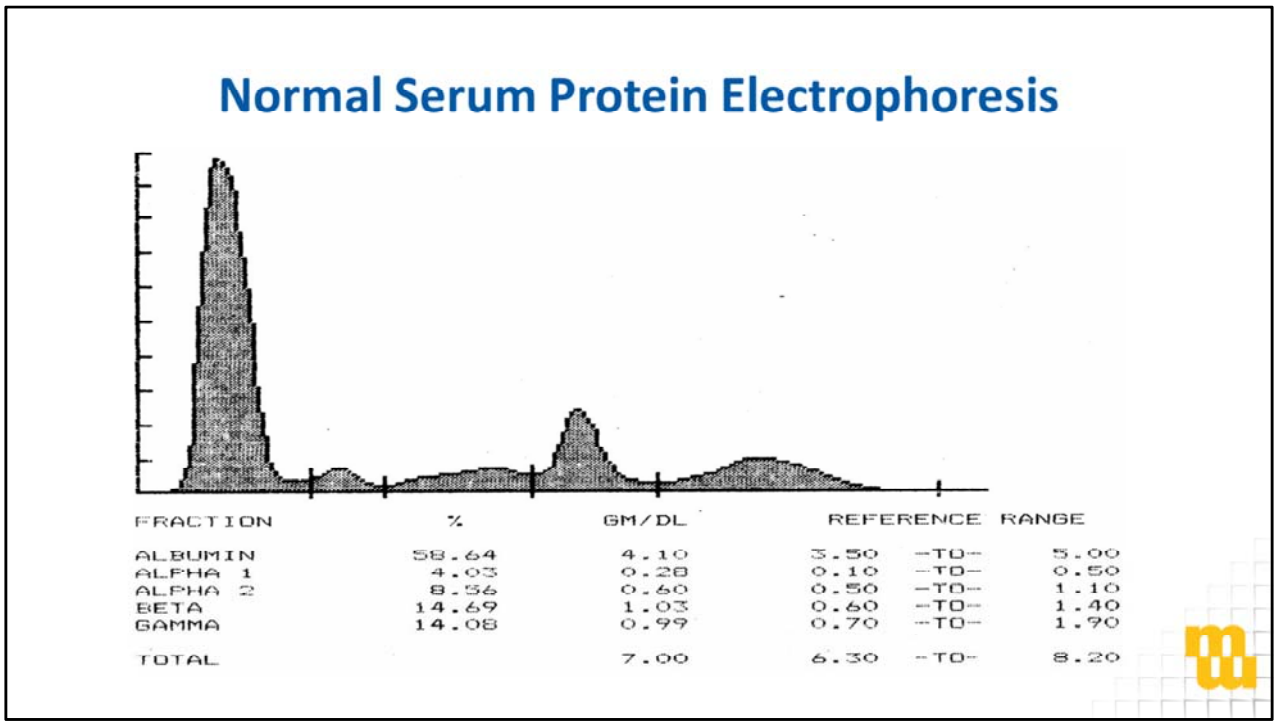
This is the Revised-ISS scoring for multiple myeloma to report from the International Myeloma Working Group (IMWG). These are the old criteria on the top which are based on the beta-2 microglobulin as well as an albumin. For patients with high beta-2 greater than 5.5 mg/L or less than 3.5 mg/L, we now begin to stratify so those patients who are stage 1 have less than 3.5 mg/L on the beta-2 and normal albumin. The stage 3's have greater than 5.5 mg/L and the stage 2's are in between, neither 1 nor 3. Now, there is a new way of staging. This came out in 2015. This is based on cytogenetic and laboratory features. So, for stage 1, these are patients who have no risk factors. They do not have a high LDH nor do they have ISS 2 or 3, and do not have t(4;14) or t(14;16) or deletion 17 abnormalities on cytogenetic analysis by interphase FISH. You can see here that the patients who are neither 1 nor 3, and 3 are ISS 3 and high-risk cytogenetic features by iFISH or a high LDH. This high LDH bad cytogenetic high burden disease population is about 10%; the neither 1 nor 3, the stage 2's, are about 60%; and the stage 1's are about 28%. This is very important to see because the progression-free survival varies from 24% to 36% to 55%, and the 5-year overall survival ranges from 40% to 62% to 82%. So, this is very helpful for us; understanding risk and prognostication and then tailoring our therapy to be more or less aggressive depending on the patient's Revised-ISS.

Testing Strategies throughout the Myeloma Disease Lifecycle



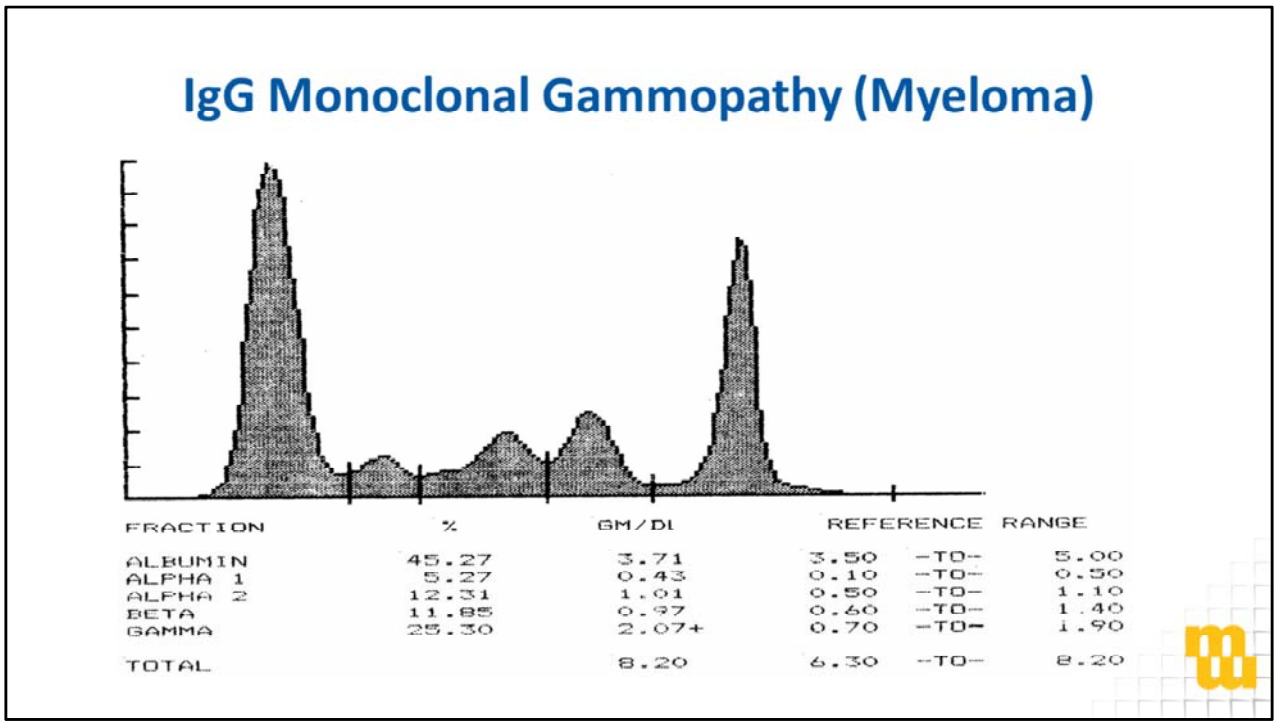
This is the proposed algorithm for reclassifying smoldering and active myeloma, it recapitulates some of the things we talked about earlier. On the right-hand side, you will see high-risk MGUS. These are patients who have less than 10% plasma cells and can be observed. In the middle are patients with no CRAB criteria, but they have greater than 10% clonal plasma cell and/or M-protein that is greater than 3 g/dL or 30 g/L. For those who have greater than 10% going down, if the serum-free light chain ratio is greater than 100 or less than 0.01, these would be patients you would consider as requiring treatment because they have a myeloma-defining event. If on whole body MRI, there is greater than one focal lesion, or in other words two or more focal lesions, these would also be patients to be considered for therapy. We're now beginning to define a patient population who should be considered for earlier therapy so as to prevent them from developing skeletal-related events, hypercalcemia, or renal failure, and thus having a major impact on their quality of life.

Testing Strategies throughout the Myeloma Disease Lifecycle



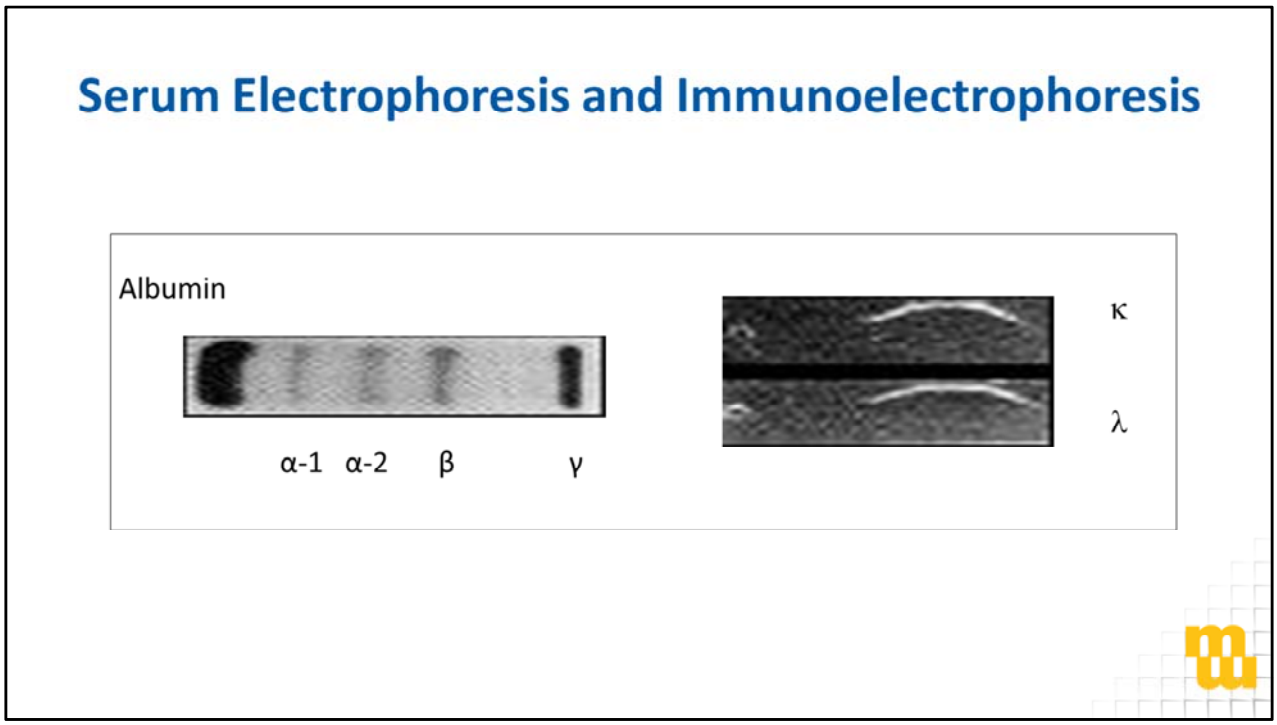
Now, this is a serum protein electrophoresis. I took this from one of our patients who was actually a normal patient who did not have myeloma. On the far left, you will see the albumin peak, and then it goes alpha-1, alpha-2, beta, and then gamma is on the far right. It is a gently sloping hill.

Testing Strategies throughout the Myeloma Disease Lifecycle



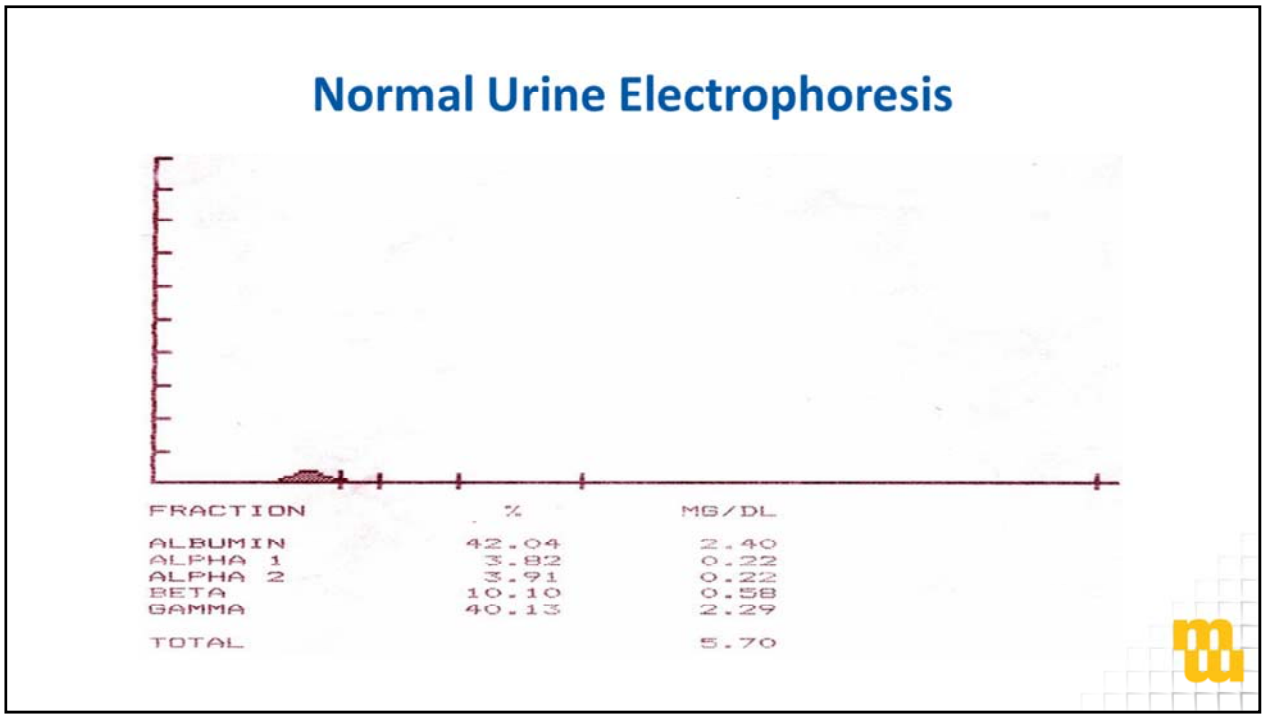
This is a patient now who has a monoclonal gammopathy. So, again you see on the far left albumin, alpha-1, alpha-2, beta, but now you will see in the gamma region the spike, and this is where the terminology M-spike comes from. This is about 2 g/dL, and so, this is somebody who is developing myeloma.

Testing Strategies throughout the Myeloma Disease Lifecycle



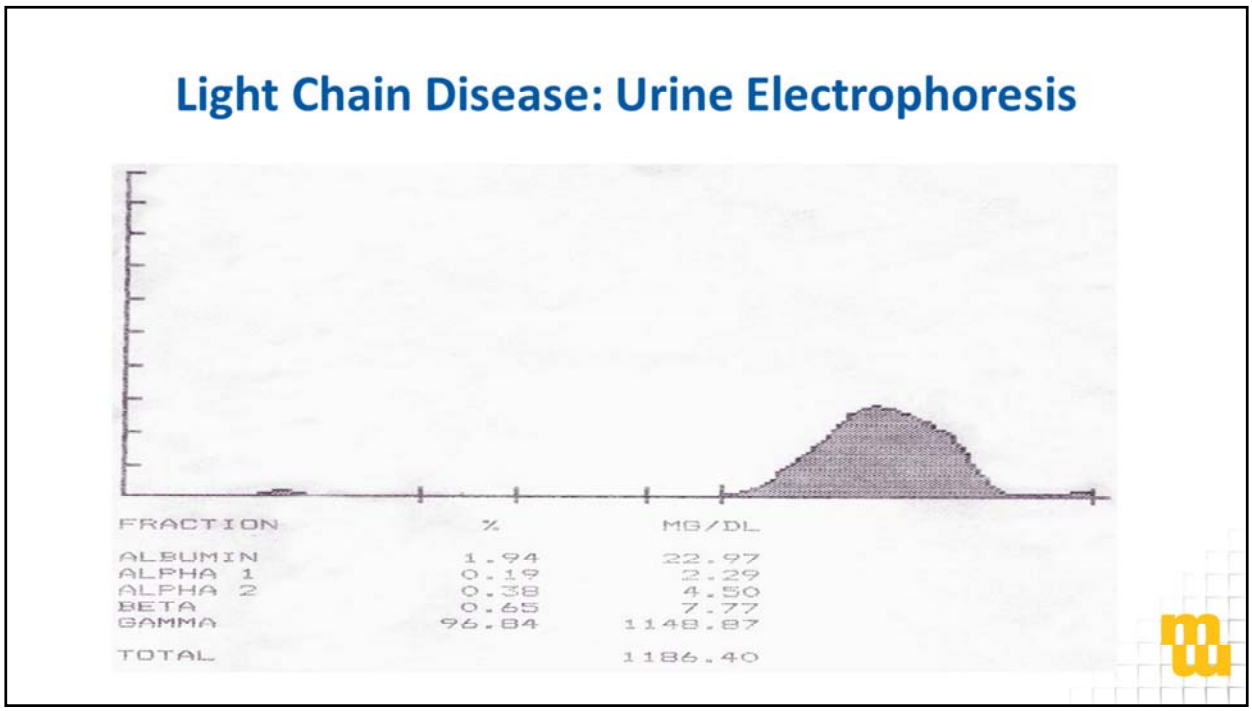
This is how those diagrams are drawn from. Here on the left-hand side, you will see serum that has been run through an electrophoresis gel. Again on the far left, there is albumin, then alpha-1, alpha-2, beta, and then gamma on the far right. This is then put through a dense photometer and then allows us to develop a peak to see the quantification of the amount of protein in each peak. On the right-hand side is a kappa/lambda study for immunoelectrophoresis. The top is kappa, the bottom is lambda, and you can see the peaks that are seen. This is useful in that most patients have about 60:40 ratio of kappa to lambda, and if you see only one (in other words that is restricted to kappa or lambda) that defines a monoclonal protein.

Testing Strategies throughout the Myeloma Disease Lifecycle



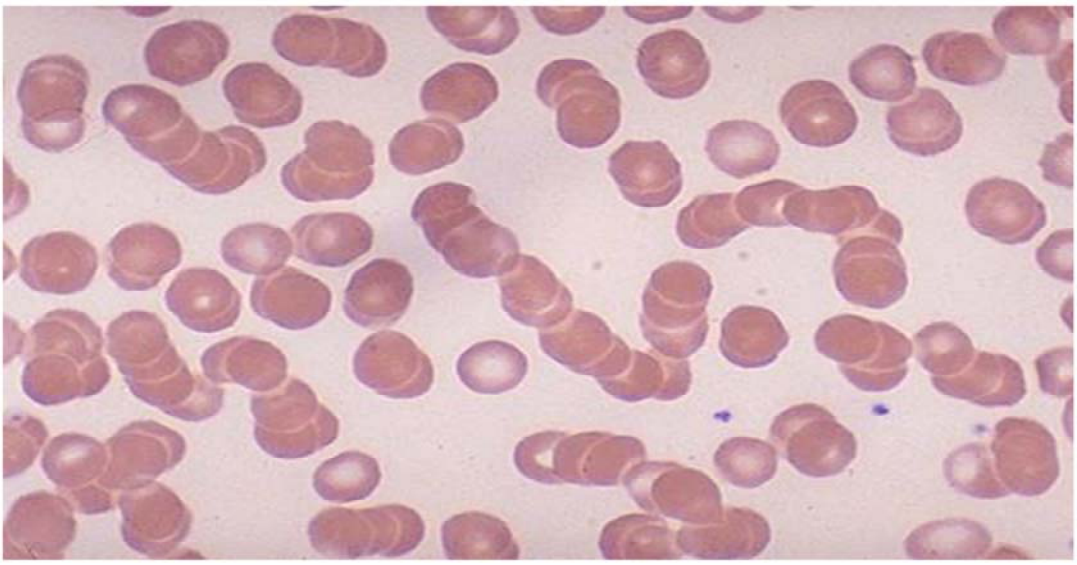
Now, this is a normal urine electrophoresis over 24 hours. You will see there is a tiny amount of albumin on the far left, a little peak.

Testing Strategies throughout the Myeloma Disease Lifecycle



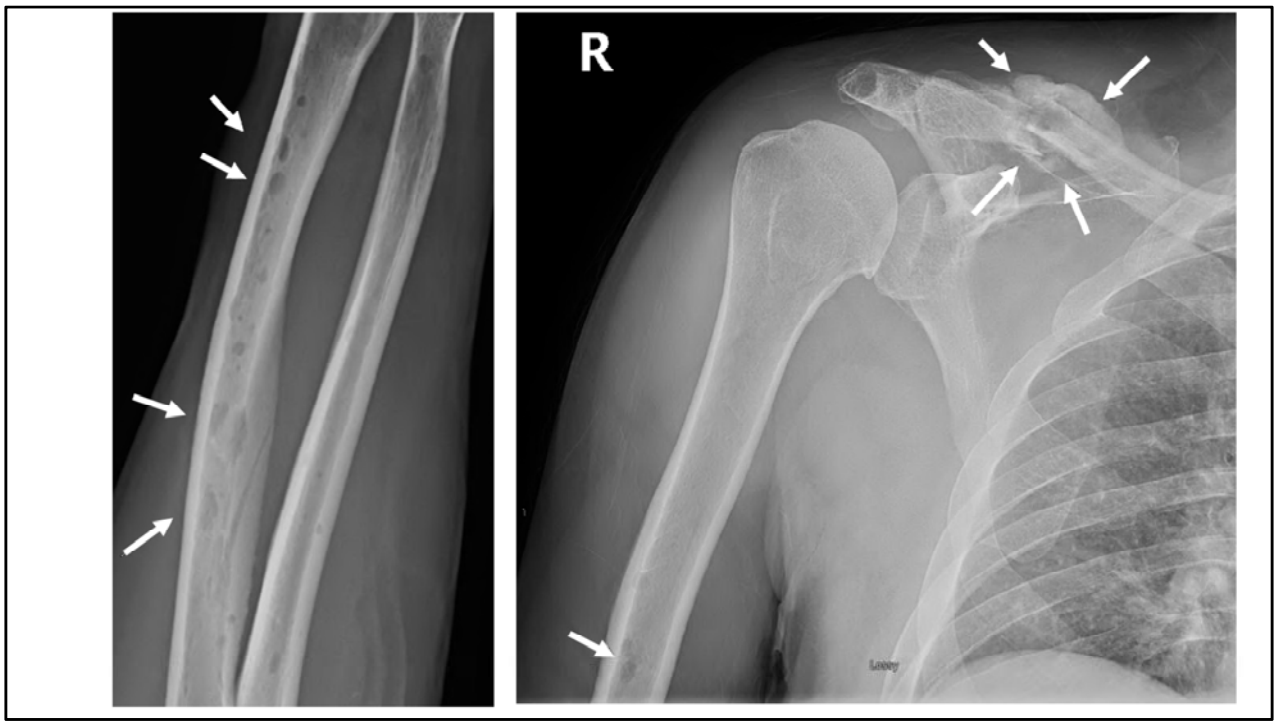
Then here is a patient with light chain disease where you will now see in the far right a large peak, which are the light chains being spilled in the urine. If you have a patient with nephrotic syndrome, you will see a lot of albumin or if you've got glomerular leak, you will see a lot of immunoglobulin being passed through; again because you are spilling protein due to the fact that the glomeruli are no longer filtering out larger proteins.

Rouleaux Formation



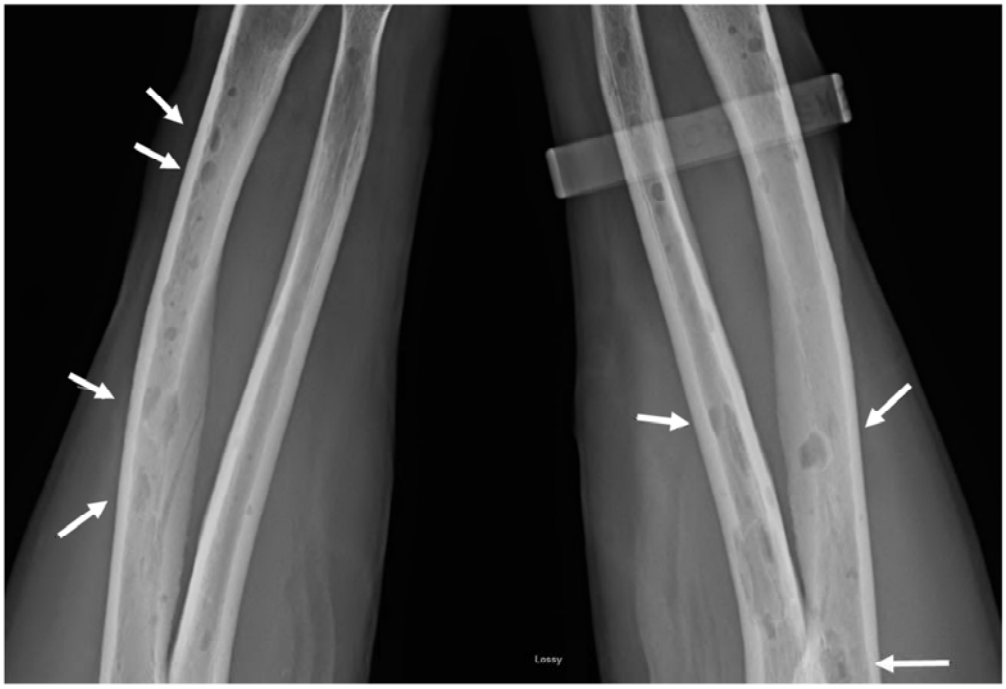
This is something for those of you who took hematology classes in medical school. You will see the rouleaux formation. We do not use this now, it is more for historical purposes, but you will see the red cells stack like coins flipped over. This is due to the high protein in the blood that causes the cells to aggregate together when they are made into smears for CBC examination.

Testing Strategies throughout the Myeloma Disease Lifecycle



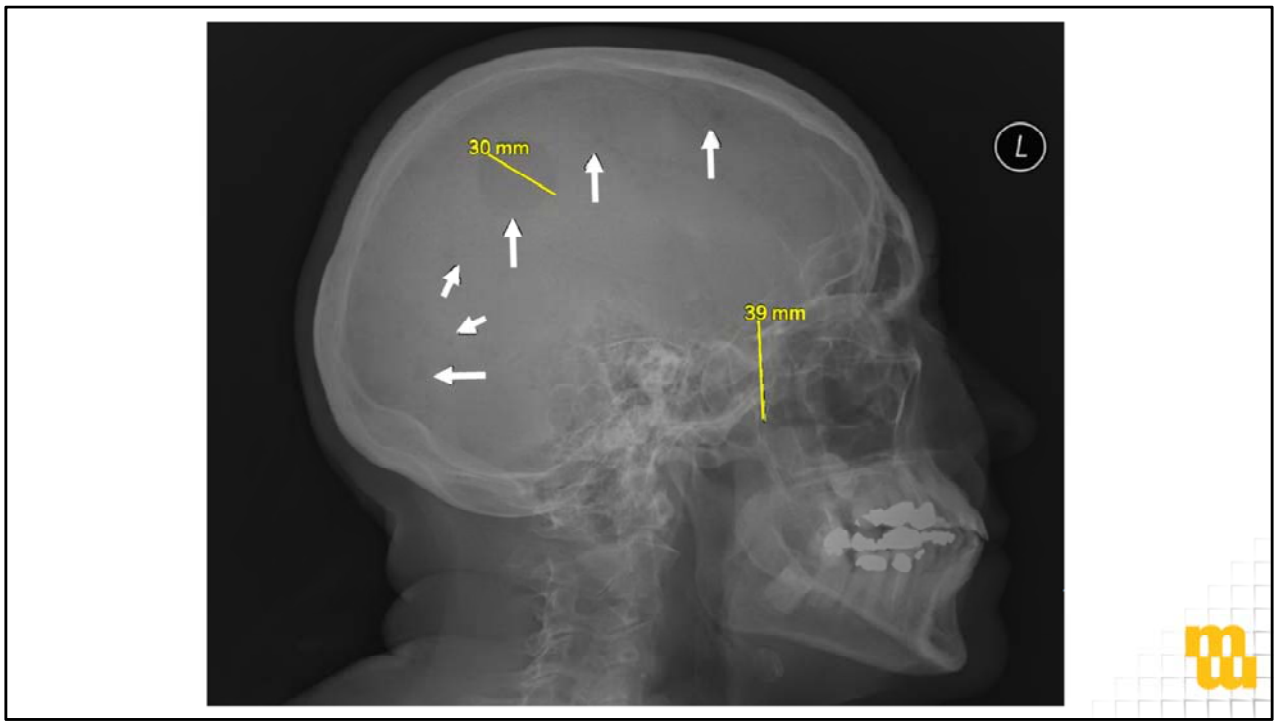
You can see a patient here, on the left-hand side, you will see arrows pointing to holes in the patient's arm bone showing lytic lesions. Then on the right-hand side, it is hard to see, but on the clavicle, you will see arrows pointing to it, and the clavicle is misaligned, and the reason why it is misaligned is that this patient had a clavicular fracture and he did not even know it. That will sometimes happen in non-weight-bearing bones. Patients will fracture things, and they may not even realize it until you actually do the skeletal survey.

Testing Strategies throughout the Myeloma Disease Lifecycle



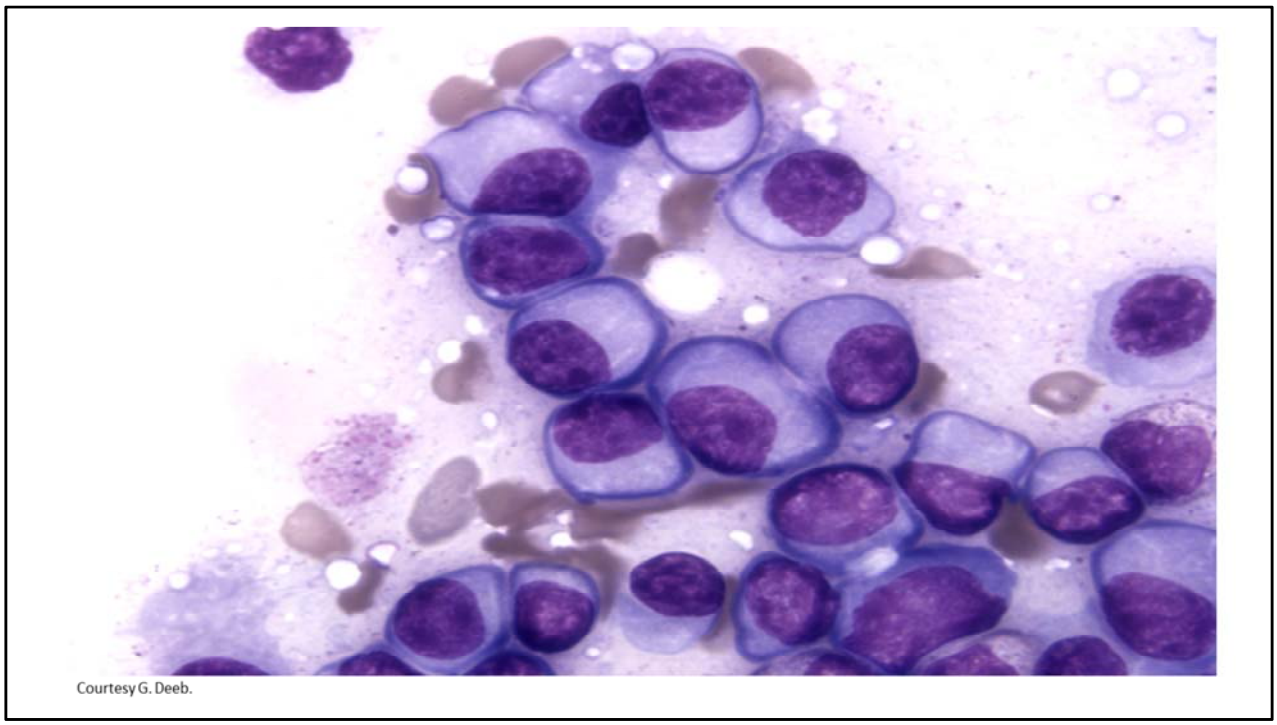
Here again are more lytic lesions as seen by the black punched-out lesions in the long bones. You worry about this in places such as the femur, where you have now weight-bearing long bones that can collapse due to the lytic lesions and these may need to be addressed orthopedic-wise to prevent a major catastrophe for the patient.

Testing Strategies throughout the Myeloma Disease Lifecycle



You can see it is 30 mm. You will see a very faint shadow that has an arrow pointing to it. It is a large 30 mm lesion in the calvarium. You will see some other lesions that are punched out and the skull films are often commonplace to see the lytic lesions in multiple myeloma.

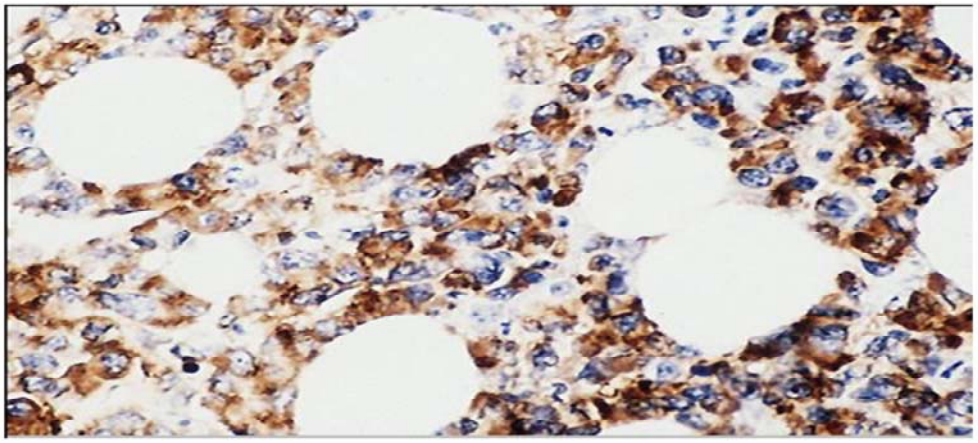
Testing Strategies throughout the Myeloma Disease Lifecycle



Here are the evil cells themselves. These are plasma cells. They have an eccentric nucleus and then a grayish white cytoplasm. The cytoplasm is filled with immunoglobulin, and with special scans, you can actually see the immunoglobulin within the cytoplasm.

Testing Strategies throughout the Myeloma Disease Lifecycle

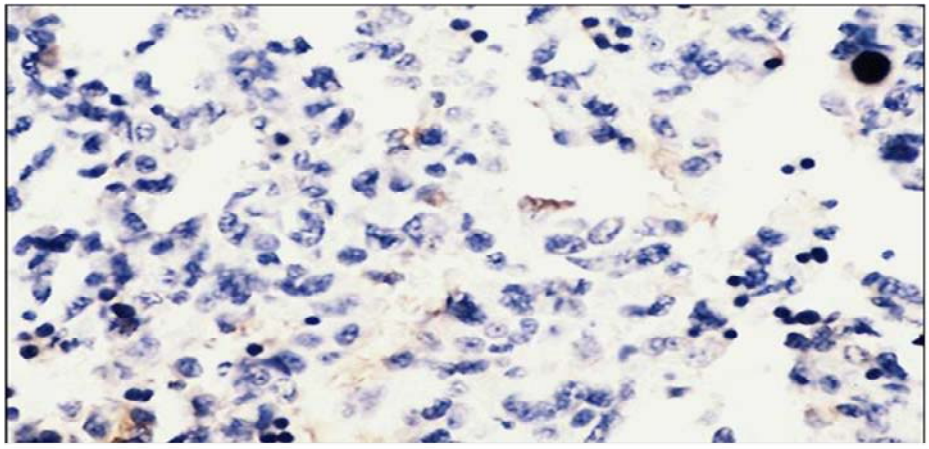
Bone Marrow Kappa Stain



Here is a kappa stain where the pathologist has stained it for kappa only. You can see that the plasma cells in this case are all stained brown, in other words they are kappa restricted. If this were a polyclonal situation, you would see a mix of both kappa and lambda.

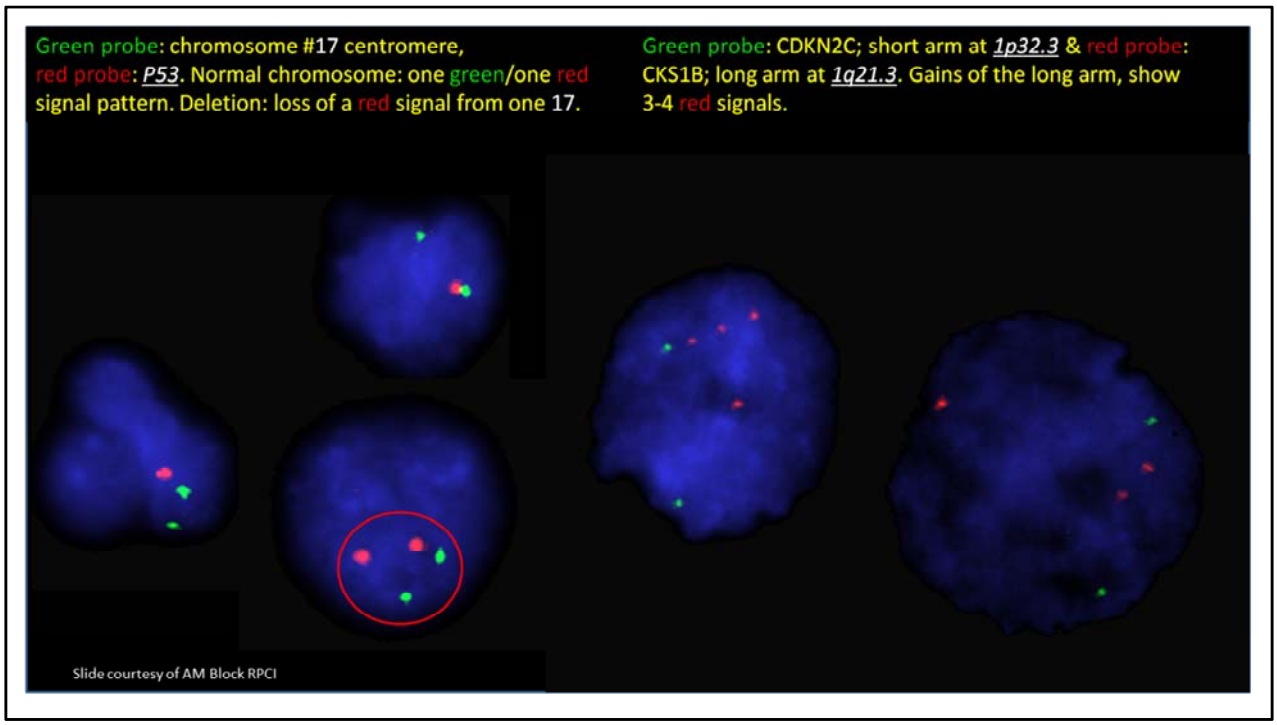
Testing Strategies throughout the Myeloma Disease Lifecycle

Bone Marrow Lambda Stain



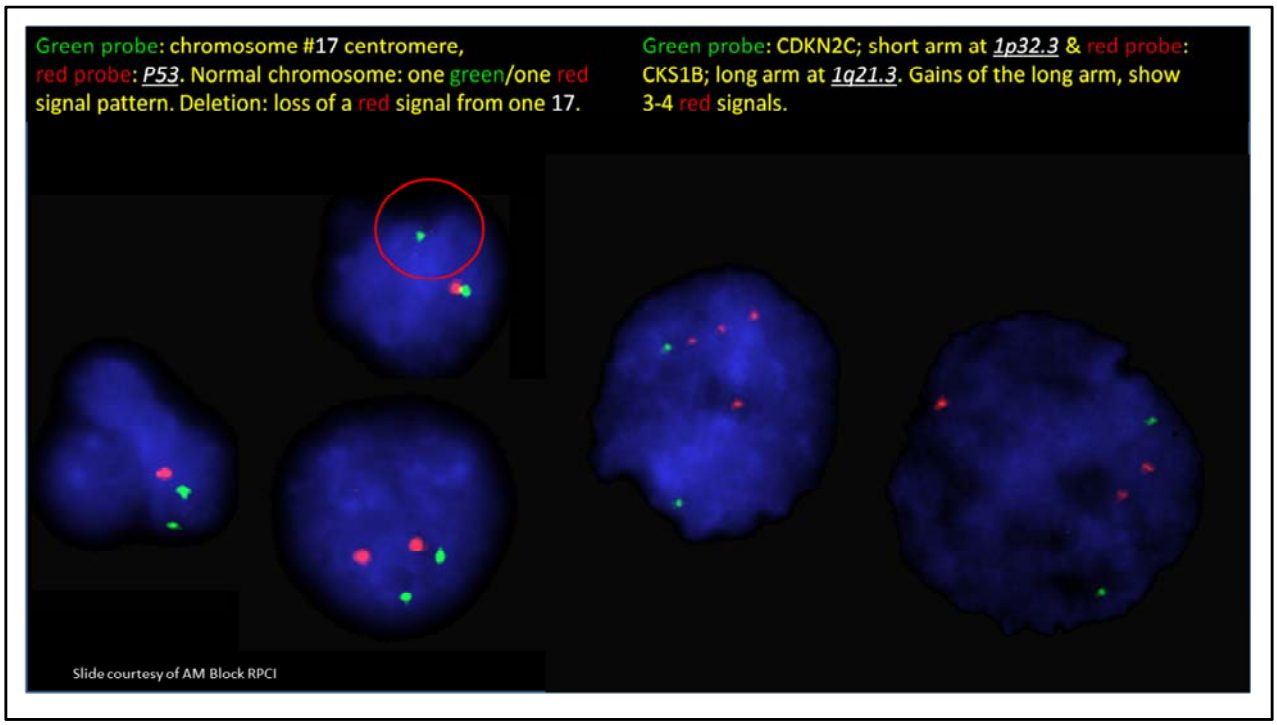
Here is the counter stain with lambda, showing that there is an absence of lambda. Why? Because these plasma cells are almost exclusively kappa.

Testing Strategies throughout the Myeloma Disease Lifecycle



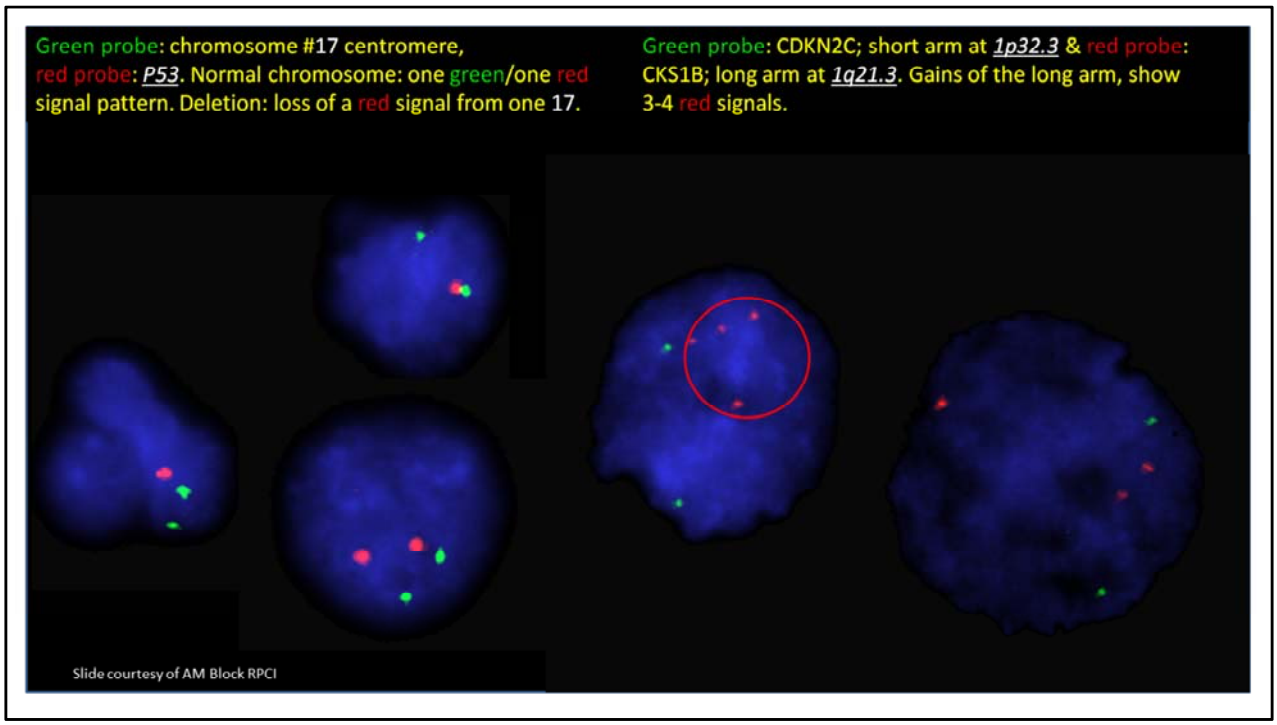
Now, this is FISH, and I show these slides because it is kind of interesting to see how FISH takes place. What the cytogeneticist does is develops probes. In this case, the green probe is to the centromere of chromosome 17. The red probe is to the p53 location on chromosome 17. So, normally, what you expect to see is one green and one red signal for each chromosome, so two red signals and two green signals. That is a normal pattern.

Testing Strategies throughout the Myeloma Disease Lifecycle



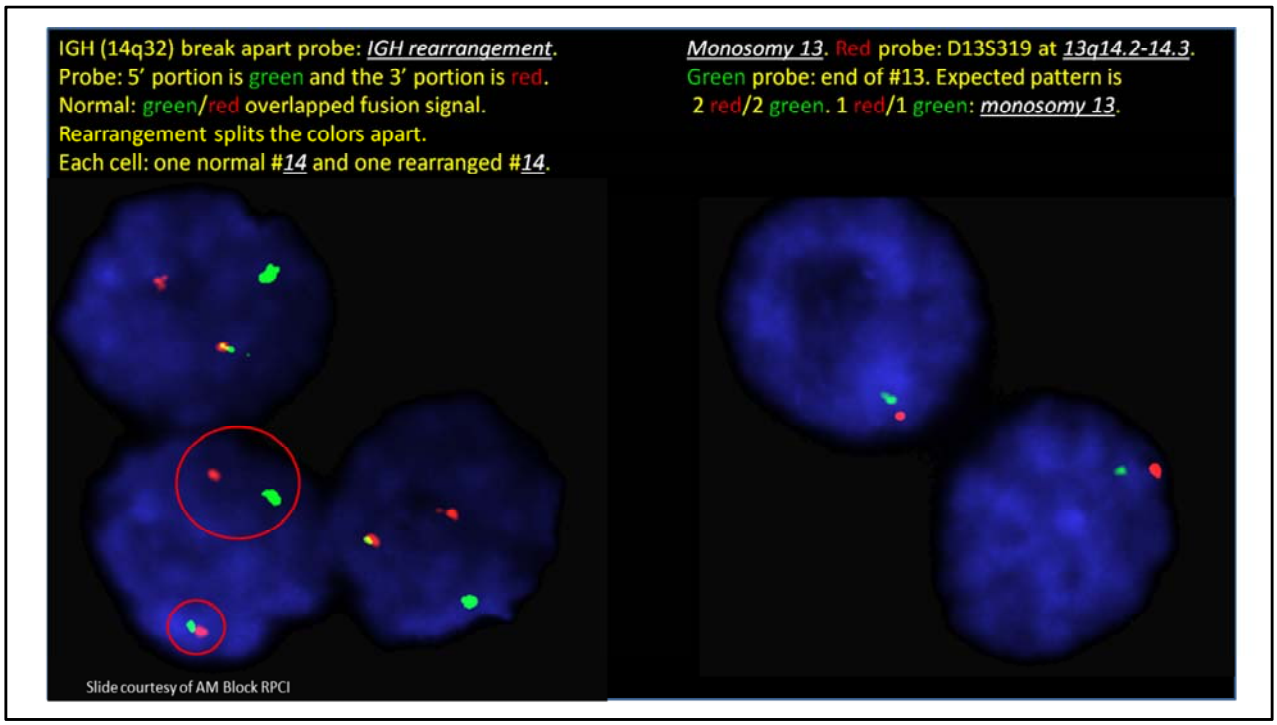
But if you see now the loss of the red signal, this is the p53 deletion. The red signal is gone. You can see the red and green signal together on the normal chromosome, but the abnormal chromosome has the deletion. On the right-hand side, we now see a green probe for CDKN2C. It is the short arm at 1p, and the red probe is CKS1B which is the long arm of 1q.

Testing Strategies throughout the Myeloma Disease Lifecycle



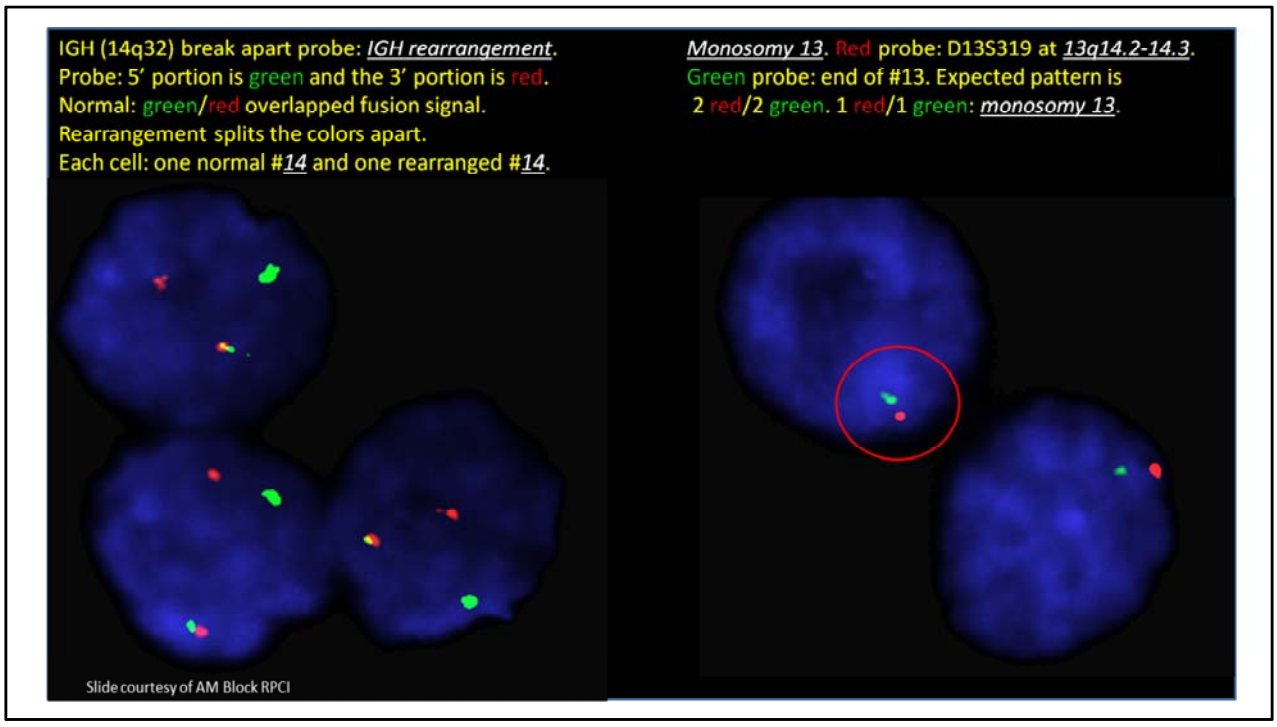
Gains of the long arm show three to four signals. You can see here this is a 1q+ where you now have four signals on the interphase FISH.

Testing Strategies throughout the Myeloma Disease Lifecycle



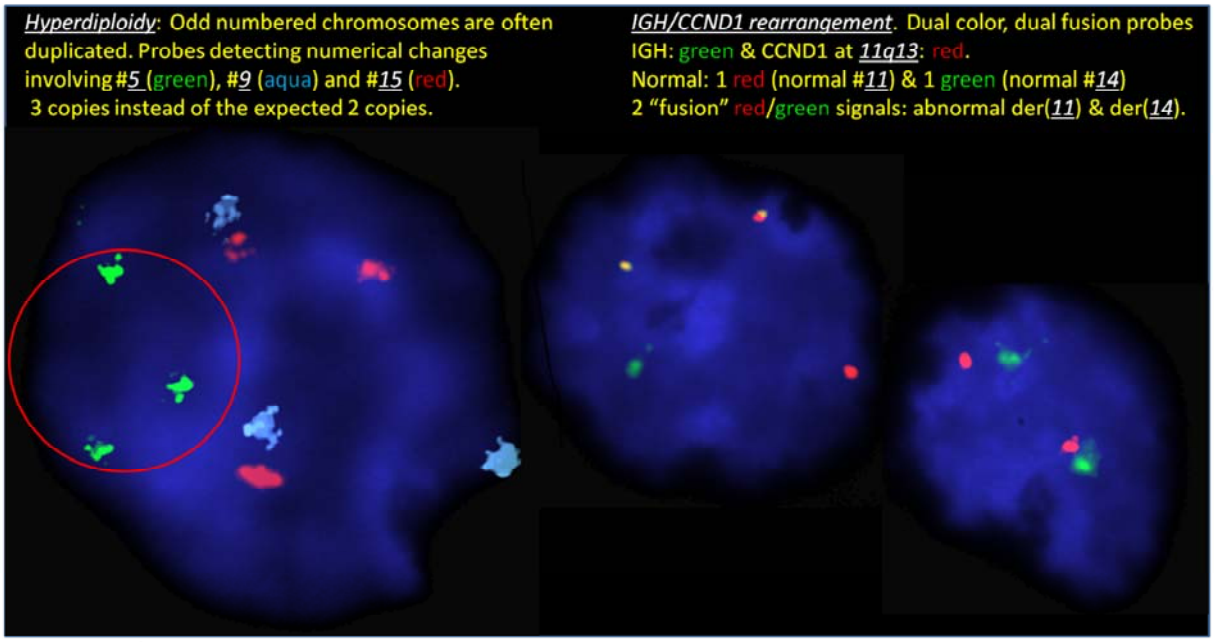
This is the immunoglobulin heavy chain rearrangement 14q. The 5 prime portion is green and the 3 prime portion is red. So, normally, you will see a green-red overlap fusion signal which you see right there at the bottom of the fusion signal. When they pull apart with the red and the green being separated, that is the break in this region, so you know that the heavy chain has been rearranged.

Testing Strategies throughout the Myeloma Disease Lifecycle



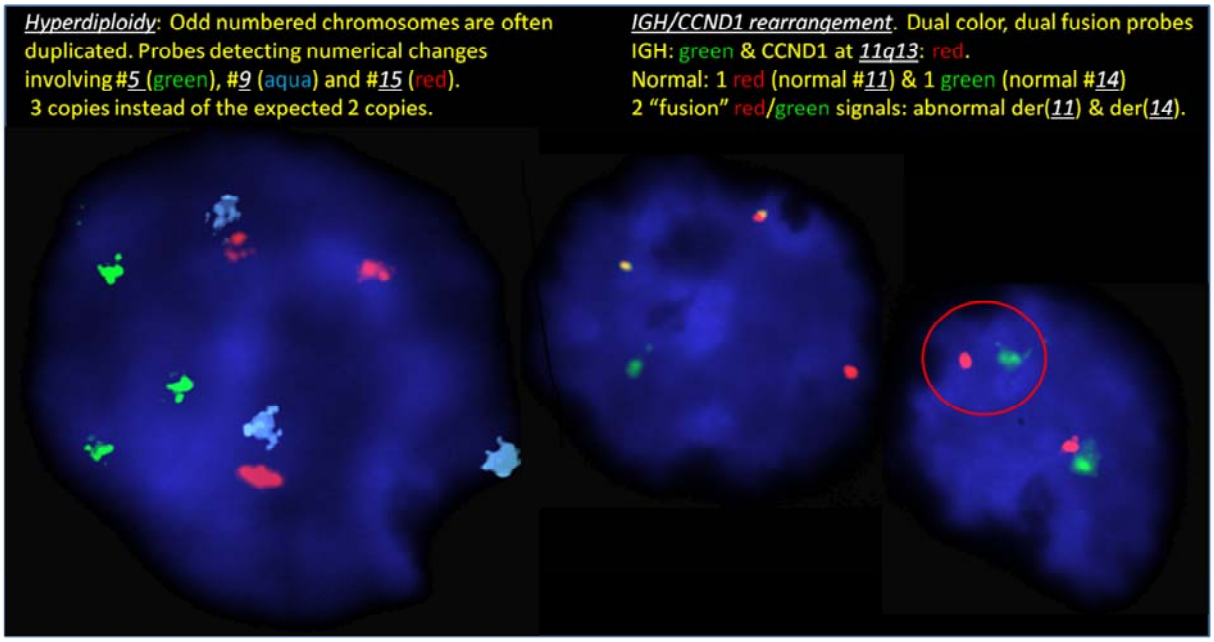
On the right-hand side , we do not have a normal cell, but here, you would expect to see two green signals and two red signals showing a pattern for chromosome 13, and you only see one green and one red signal showing that this is a patient who has monosomy 13.

Testing Strategies throughout the Myeloma Disease Lifecycle



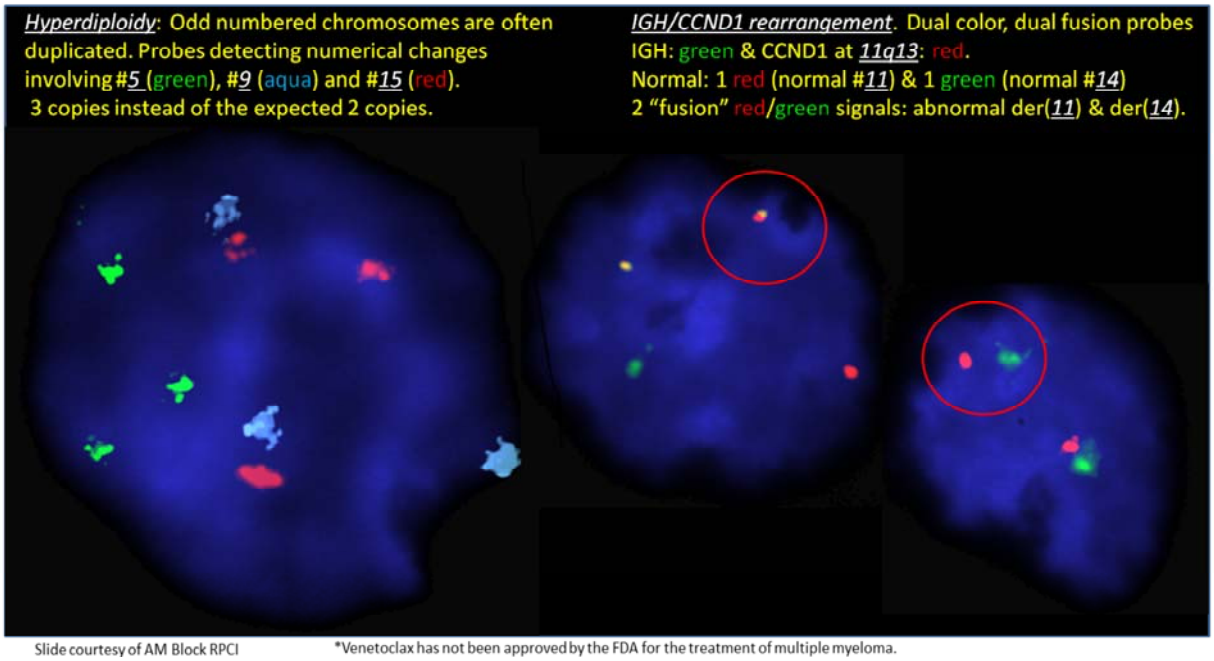
Hyperdiploidy is another manifestation of myeloma. Often the odd number chromosomes are duplicated. So, probes detecting three chromosomes, 5, 9, and 15 are shown; 5 is green, 9 is aqua, and 15 is red, and as you can see here, there are three copies of chromosome 5, thus demonstrating the trisomy.

Testing Strategies throughout the Myeloma Disease Lifecycle



On the right-hand side, we have another immunoglobulin heavy chain rearrangement. This is with chromosome 11. IGH is in green, CCNV1, which is a marker for chromosome 11q13 (that's the location on 11) is in red, and normally what you will see is one red and one green.

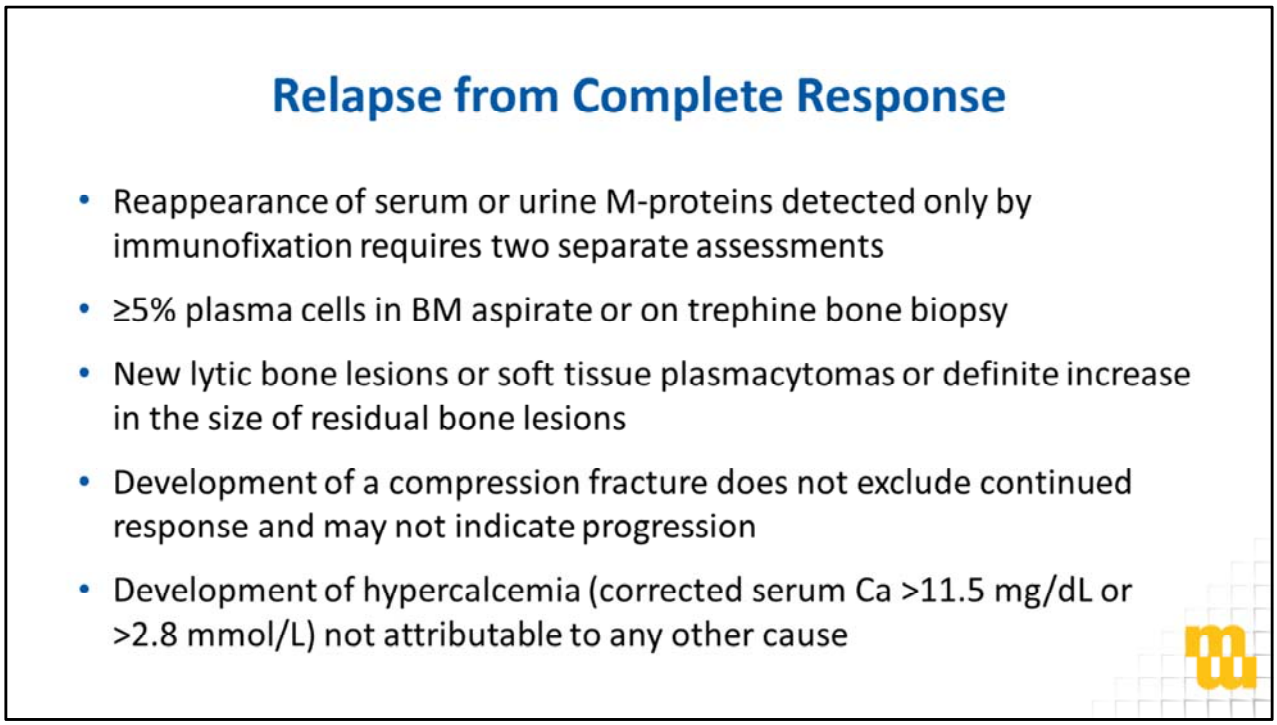
Testing Strategies throughout the Myeloma Disease Lifecycle



What we will see abnormally is you will see a fusion . So, when you have a fusion of the signals as manifested by the dots that are on top of each other, that is the t(11;14). Whereas, if you see the two signals separated that is normal. This is actually very important now that we venetoclax,* as an aside. Venetoclax targets patients who have 11;14 chromosome abnormality, and this will hopefully be something that we will be utilizing for this patient populations. We are beginning to see how important these cytogenetic abnormalities are with regard to prognosis and assigning therapy.

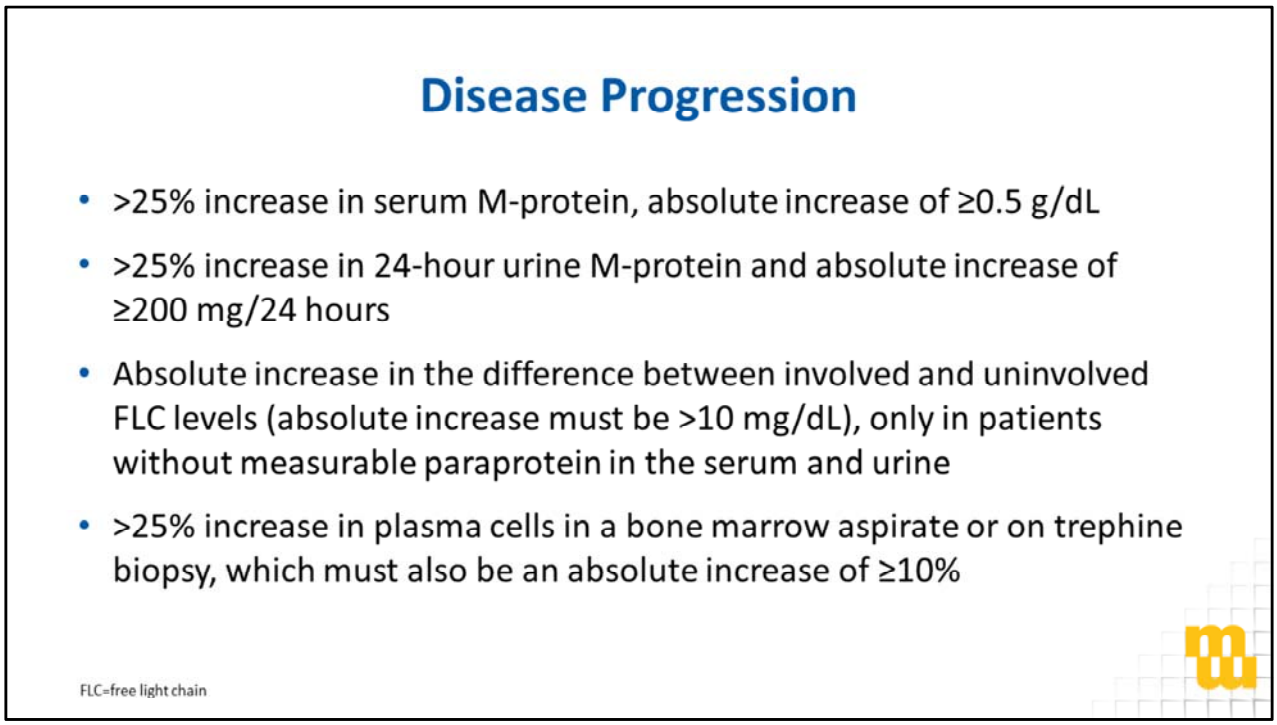
**Venetoclax has not been approved by the FDA for the treatment of multiple myeloma.*

Testing Strategies throughout the Myeloma Disease Lifecycle



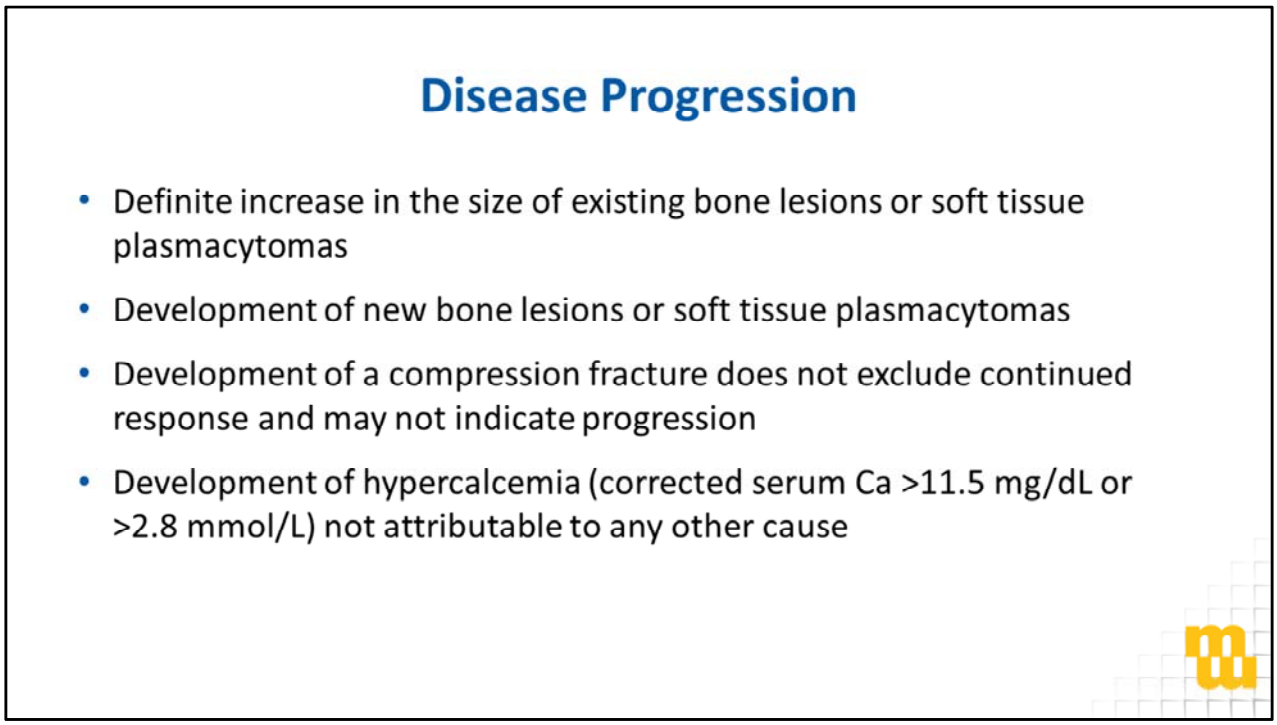
I am going to finish with talking about relapse and progression. Relapse from CR is the reappearance of serum or urine M-protein detected only by immunofixation. It requires two separate assessments, that is very important to really confirm progression/or relapse. You want to have greater than 5% plasma cells in the bone marrow aspirate or biopsy. There are new lytic bone lesions or soft tissue plasmacytomas or definite increase in size of the lesion, that is another indication of relapse. A compression fracture alone does not exclude continued response; it is very important to make sure you confirm progression by another indication. Then, hypercalcemia in the absence of other cause will lead to a patient undergoing workup to look for the presence of clonal cells or clonal protein.

Testing Strategies throughout the Myeloma Disease Lifecycle



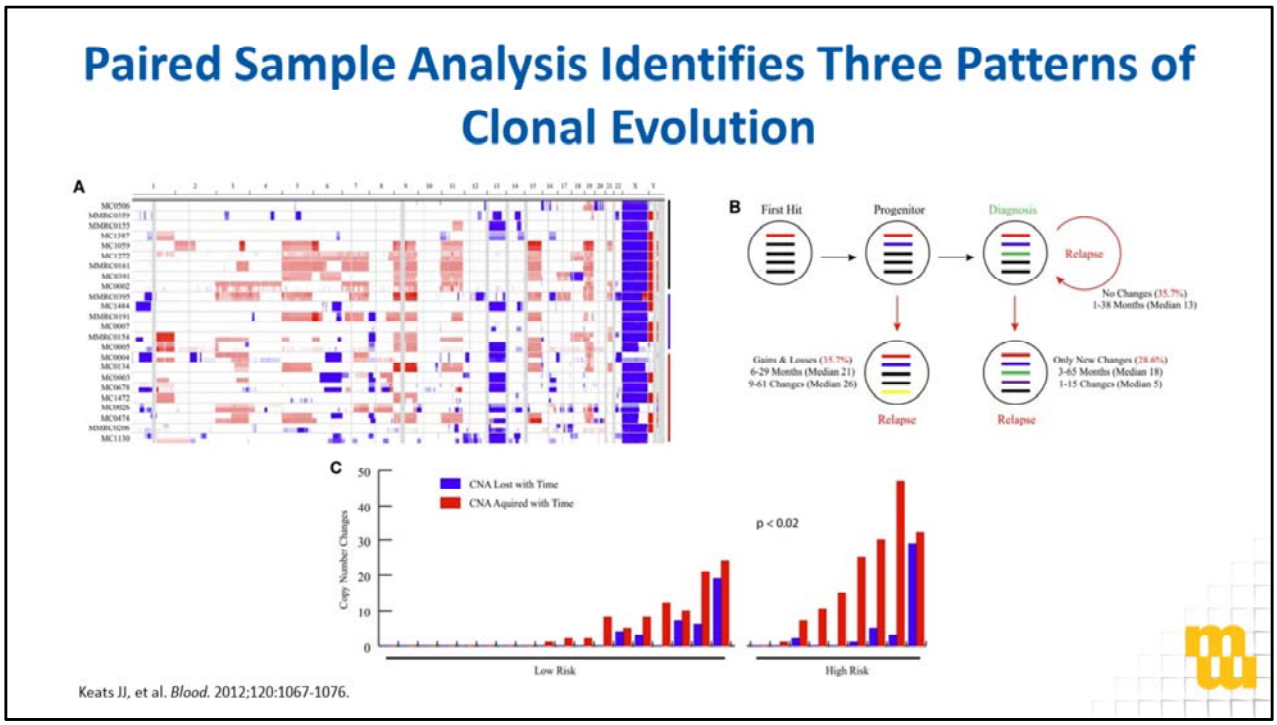
Now, progression is a little different. This is a higher volume of disease. So, the relapse will be from a complete remission, whereas disease progression is a higher amount. It is a greater than 25% increase in serum M-protein, an absolute increase of 0.5 g/dL, and the 25% increase in urine protein, and an absolute increase of 200 mg over 24 hours, depending on what you are measuring. For a free light chain ratio, there needs to be an absolute increase of greater than 10 mg/dL, but this is only in patients who do not have measurable paraprotein and serum in the urine. In the majority of patients who either have urine or serum protein that could be measured, there also should be a 25% increase in plasma cells in the bone marrow aspirate or biopsy, and it needs to be an absolute increase of at least 10%.

Testing Strategies throughout the Myeloma Disease Lifecycle



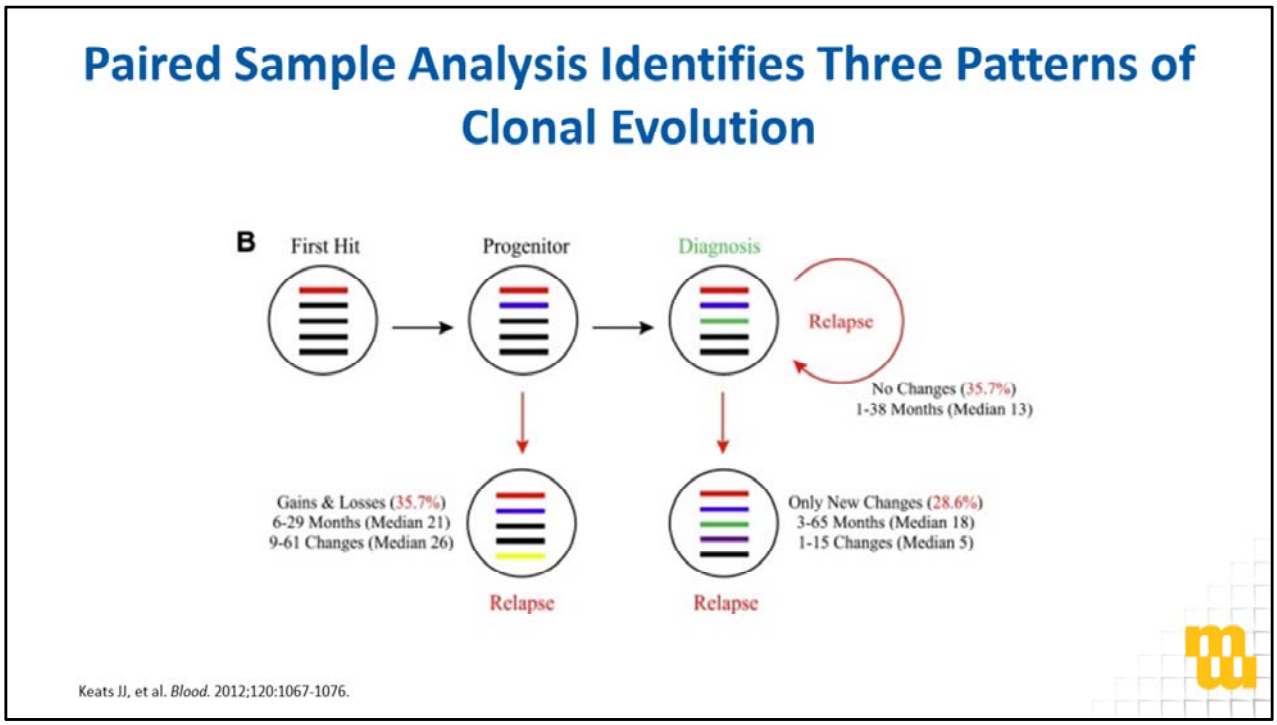
As mentioned with the relapse and progression, we need to see an increase in the size of the existing bone lesions or soft tissue plasmacytomas, development of new lesions of plasmacytomas, and again compression fracture alone is not enough to call progression. Hypercalcemia that is not attributable to another cause should be an indication for workup to see if the patient has occult disease.

Testing Strategies throughout the Myeloma Disease Lifecycle



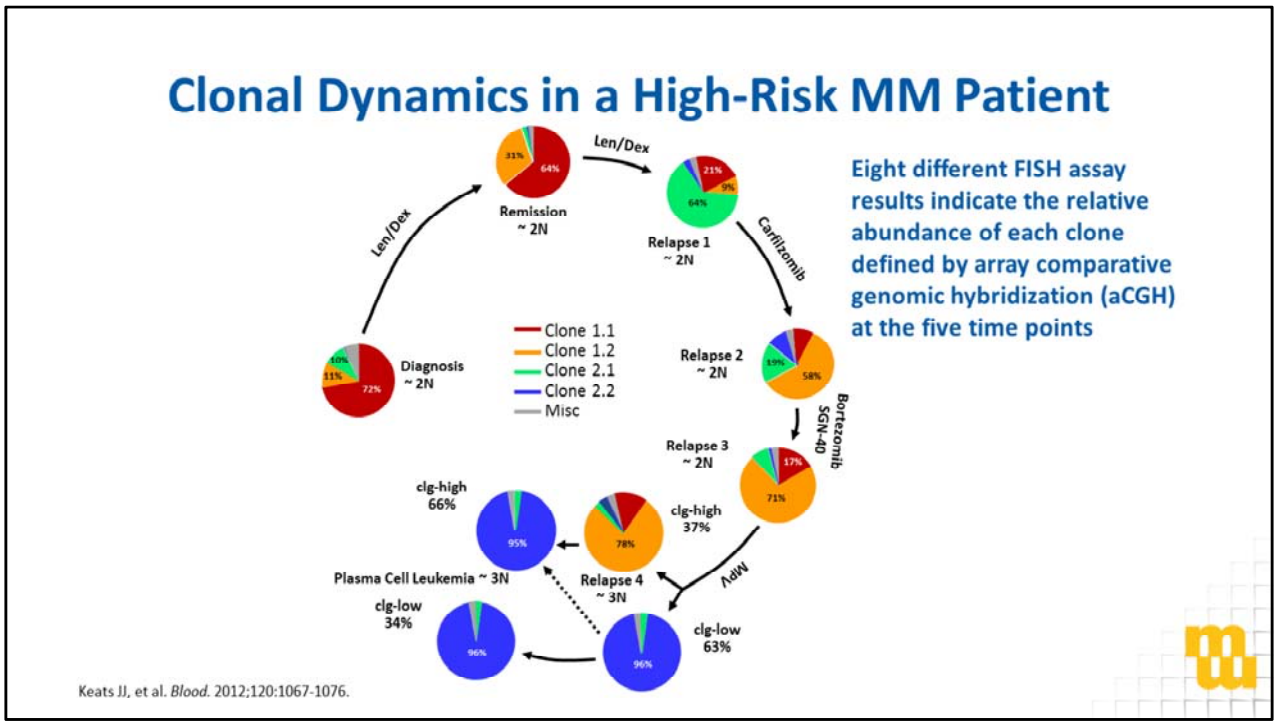
So, I am going to finish up. This is paired sample analysis from the Mayo Group, and it is a rather complicated diagram showing clonal evolution over time.

Testing Strategies throughout the Myeloma Disease Lifecycle



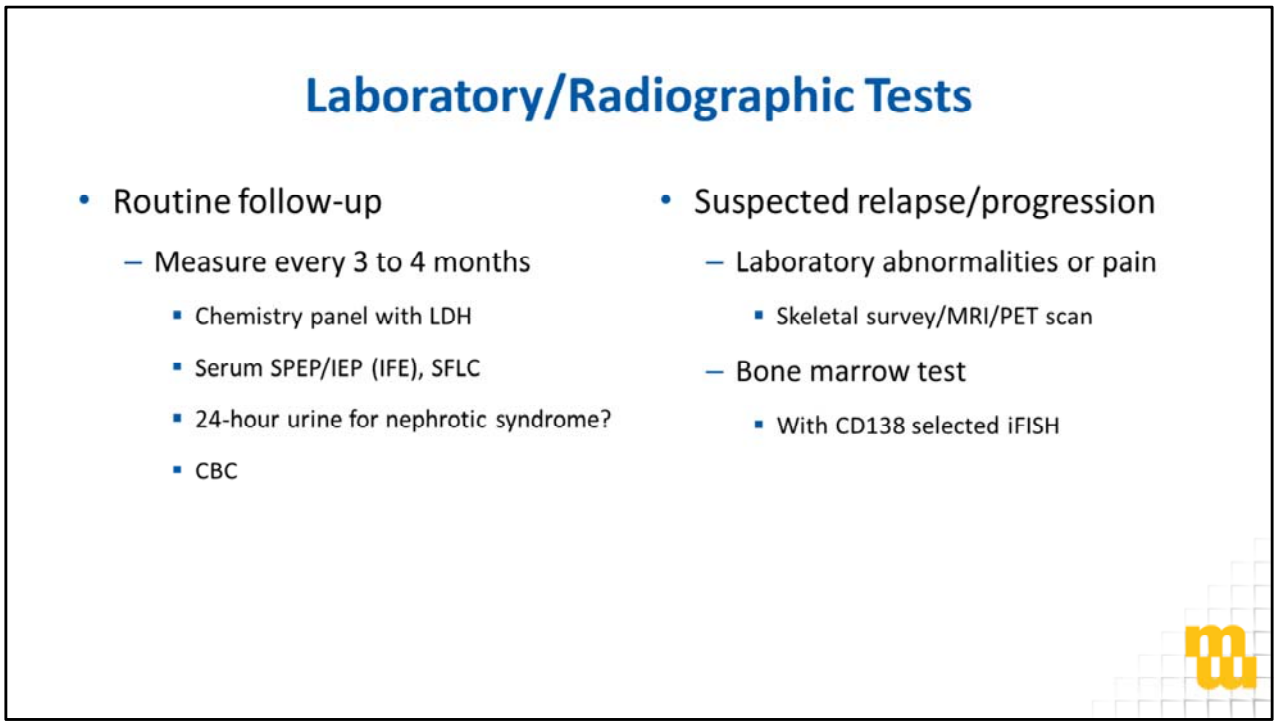
What they show here, blowing up this portion of the slide, is that it is probably a first hit that leads to a precondition, maybe MGUS, then a progenitor abnormality, and then on the right-hand side you will see diagnosis and then relapse. In other relapses they find that the same abnormalities seen at diagnosis are often seen at relapse, about one-third of the patients. And then in one-third of the patients that relapse, there will be new changes seen only in about one-third of the patients, and then on the left-hand side at the bottom, you will see both old and new abnormalities.

Testing Strategies throughout the Myeloma Disease Lifecycle



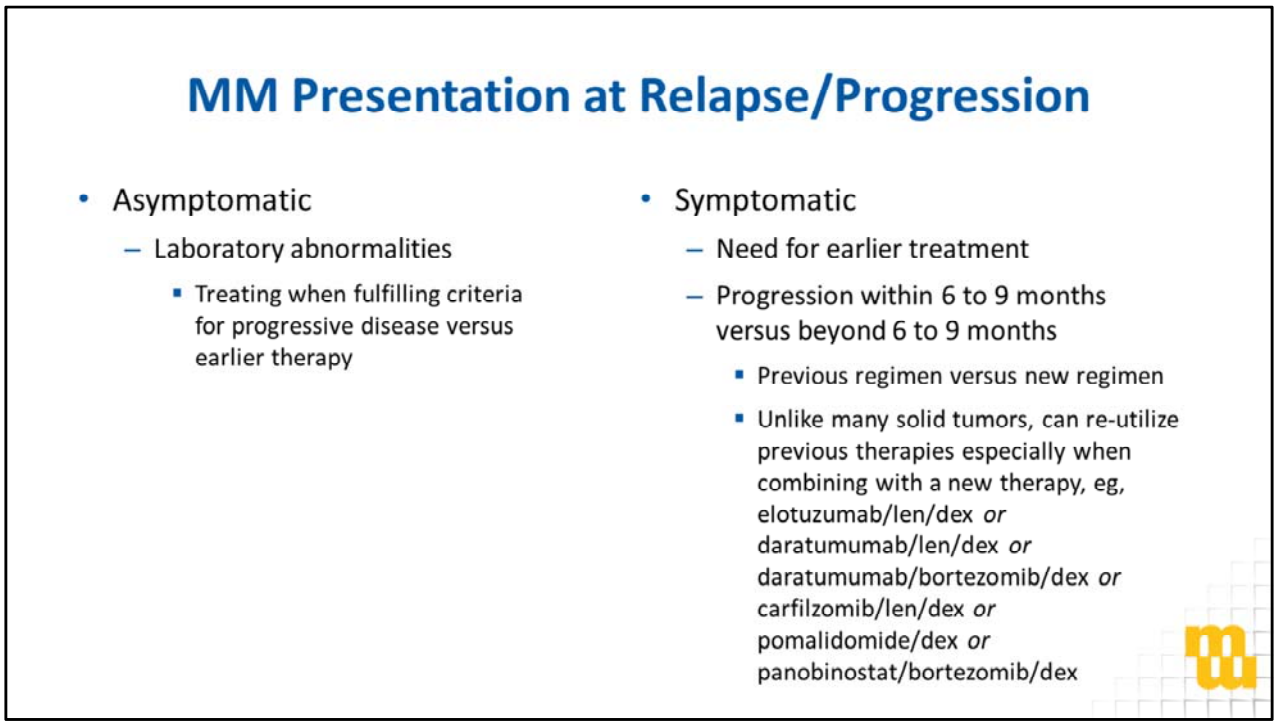
This is really demonstrated in this slide. This is a patient who had clone 1.1 in red at diagnosis. The patient received lenalidomide-dexamethasone and then went into remission. This clone was still present, continued on it, and then at disease relapse, clone 2.1 in green was the predominant clone. The patient received a carfilzomib-containing salvage, clone 2.1 decreased but now clone 1.2 arose, and then, the patient received a bortezomib investigational drug. You will see control of disease, but then over time, you will now see a new clone 2.2 which is manifested as plasma cell leukemia. This patient had progressive disease with a completely different set of clones than what was seen at diagnosis. So, this points out the importance of considering a full workup including bone marrow aspirate for iFISH to make sure that the patient has not developed new cytogenetic abnormalities which may target therapy.

Testing Strategies throughout the Myeloma Disease Lifecycle



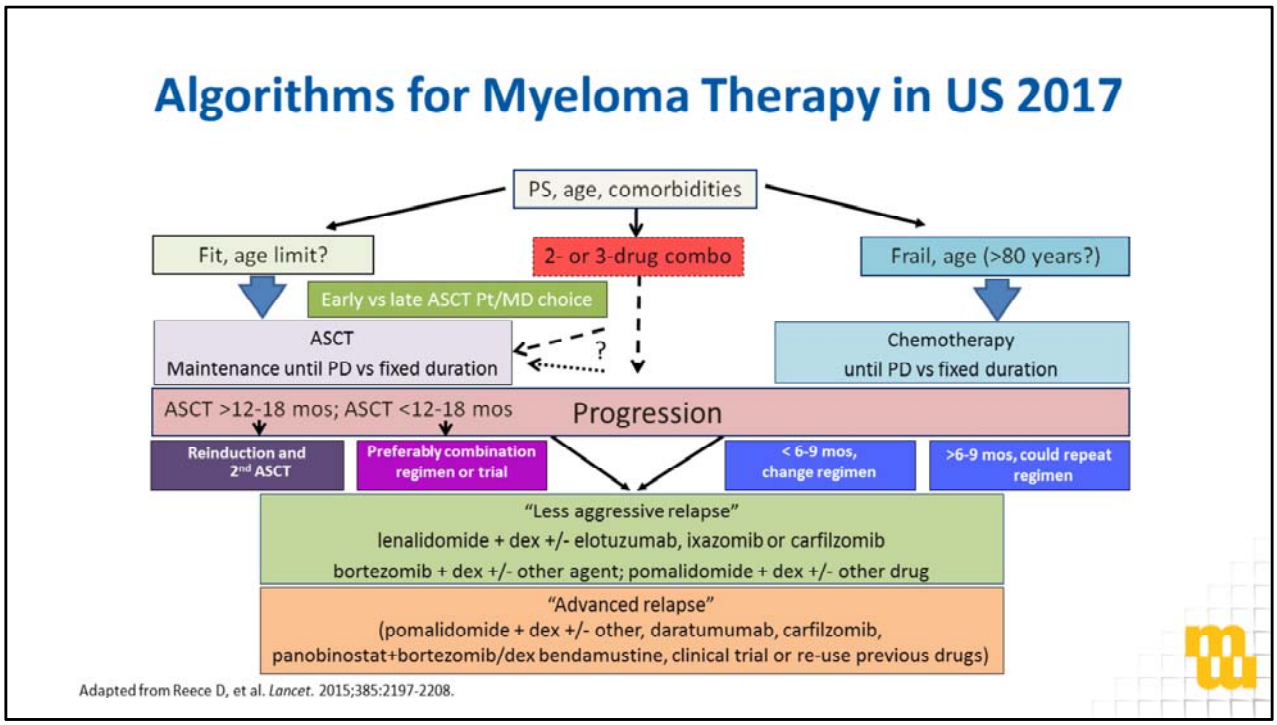
These are the laboratory and radiographic tests to consider for routine followup. On the left, you will want to measure every 3 to 4 months a chemistry panel with LDH, SPEP, immunoelectrophoresis, and serum-free light chains. Possibly a 24-hour urine, especially in somebody with nephrotic syndrome, and then a CBC. For suspected relapse to progression, we would want to look at the laboratory abnormalities that might be developing. In other words, the rising M-protein, serum-fee light chains, as well as symptoms such as pain requiring radiographic testing with either skeletal survey, or perhaps an MRI/PET scan to look for occult disease, and then a bone marrow test with CD138 selected FISH to help us guide treatment.

Testing Strategies throughout the Myeloma Disease Lifecycle



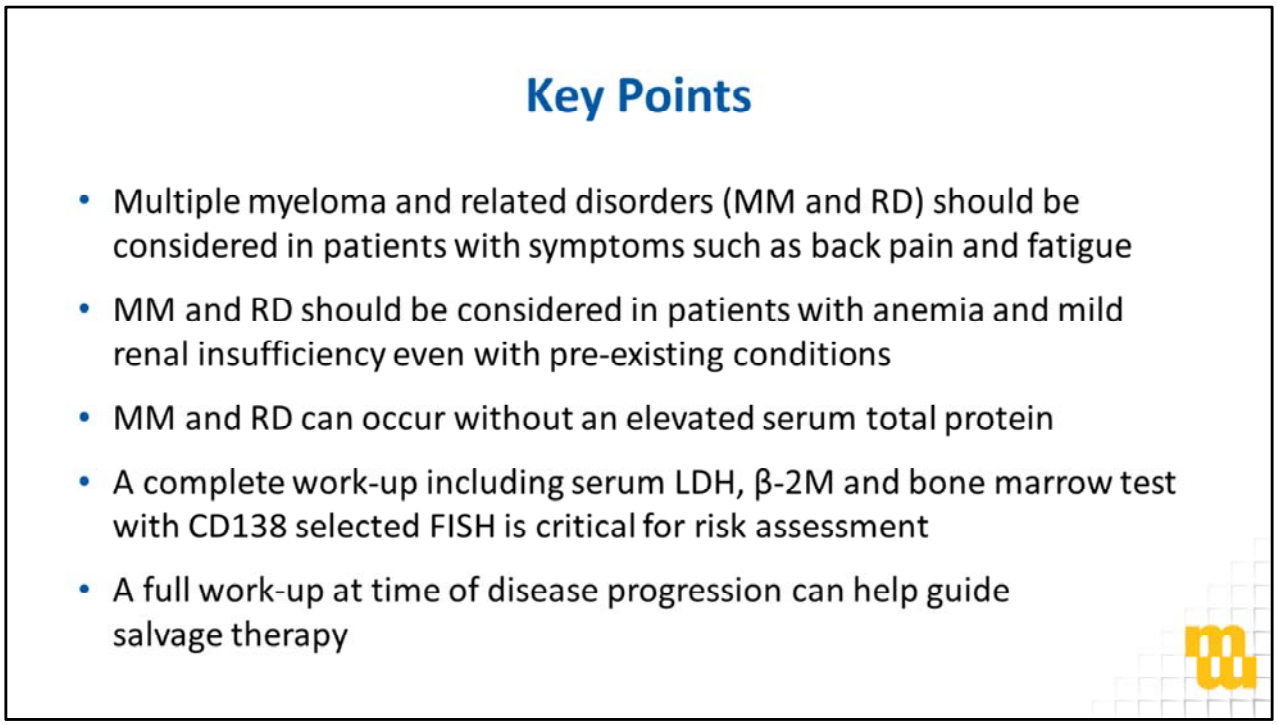
This is what we consider if we have a patient who is asymptomatic. They have laboratory abnormalities alone, do we want to treat with early disease or do we want to wait for the patient to fulfill criteria for progressive disease? At a minimum if they fulfill criteria for progressive disease, they need to be treated. If they are early on, they may be able to be watched for a few months but very carefully to make sure they do not have a rapid progression which would potentially lead to end-organ damage. If they are symptomatic, there is a need for earlier therapy. If they have had progression beyond 6 to 9 months from their last treatment, as opposed to within that time period, you may want to tailor your therapy differently. You sometimes can look at a previous regimen, especially if it has been a long time since they were exposed to the original treatment, and unlike many solid tumors, you can re-utilize previous therapies, especially when combining with a new therapy. For example, elotuzumab with lenalidomide-dexamethasone, or daratumumab with lenalidomide-dexamethasone, or daratumumab with bortezomib-dexamethasone, or carfilzomib lenalidomide-dexamethasone, or pomalidomide-dexamethasone, and panobinostat-bortezomib-dexamethasone. These are just some of the options that we now have and we are going to get better at figuring out how we can sequence all of these in controlling disease.

Testing Strategies throughout the Myeloma Disease Lifecycle



This is an algorithm which I borrowed from Donna Reece and adapted from Dr. Wahlig from *Lancet* in 2015. You will see that patients need to be considered based on performance status, age, and comorbidities. If they are fit, they can be considered for a transplant. If they are frail, older, chemotherapy until progression versus fixed duration at time of the progression, then we have to think about what regimens to use. We now have a variety of options depending on the type of relapse – aggressive or less aggressive – that may tailor our therapy.

Testing Strategies throughout the Myeloma Disease Lifecycle



So, the key points today are that multiple myeloma and related disorders should be considered in patients with symptoms such as back pain and fatigue. Myeloma and related disorders should be considered in patients with anemia and mild renal insufficiency, even those with preexisting conditions, especially with those because you do not want to ascribe renal insufficiency to diabetes or hypertension that turns out they are developing myeloma. Myeloma and related disorders can occur without an elevated serum total protein, so it is something to consider. Thus, serum-free light chains and immunoelectrophoresis should be considered. A complete workup includes a serum LDH, beta-2 microglobulin, and bone marrow test with CD138 selected FISH as very critical for risk assessment. A full workup at the time of disease progression can help guide salvage therapy.